Devi, S.
08/905293

=> fil reg; d que l1; fil caplu; d que l5

FILE 'REGISTRY' ENTERED AT 16:24:14 ON 07 DEC 1998

STRUCTURE FILE UPDATES: 6 DEC 98 HIGHEST RN 215160-44-4
DICTIONARY FILE UPDATES: 6 DEC 98 HIGHEST RN 215160-44-4

TSCA INFORMATION NOW CURRENT THROUGH JUNE 29, 1998

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Key terms

L1 3645 SEA FILE=REGISTRY ABB=ON PLU=ON IMMUNOGLOBULIN ?/CN

FILE 'CAPLUS' ENTERED AT 16:24:15 ON 07 DEC 1998

FILE COVERS 1967 - 7 Dec 1998 VOL 129 ISS 24
FILE LAST UPDATED: 7 Dec 1998 (981207/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

L1 3645 SEA FILE=REGISTRY ABB=ON PLU=ON IMMUNOGLOBULIN ?/CN
L2 75102 SEA FILE=CAPLUS ABB=ON PLU=ON L1 OR IMMUNOGLOBULIN OR IMMUNO GLOBULIN OR IG
L3 218 SEA FILE=CAPLUS ABB=ON PLU=ON L2(S)TOXIC?
L4 25 SEA FILE=CAPLUS ABB=ON PLU=ON L3(S)INHIBIT?
L5 4 SEA FILE=CAPLUS ABB=ON PLU=ON L4 AND (LEX OR LEY OR LE OR BR96 OR (BR OR CHIBR OR HBR)(W)96 OR CHIBR96 OR HBR96 OR HB10460 OR HB10036 OR HB(W)(10460 OR 10036) OR MOAB

Searcher : Shears 308-4994

OR MAB OR MONOCLON?)

=> d 1-4 .bevstr

L5 ANSWER 1 OF 4 CAPLUS COPYRIGHT 1998 ACS
AN 1998:112463 CAPLUS
DN 128:204075
TI A method for **inhibiting immunoglobulin**-induced **toxicity** resulting from the use of **immunoglobulins** in therapy and in vivo diagnosis
IN Rosok, Mae Joanne; Yelton, Dale E.
PA Bristol-Myers Squibb Co., USA
SO PCT Int. Appl., 140 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9805787	A1	19980212	WO 97-US13562	19970801
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9739688	A1	19980225	AU 97-39688	19970801
PRAI	US 96-23033		19960802		
	WO 97-US13562		19970801		

AB The present invention provides a method for **inhibiting Ig**-induced **toxicity** resulting from immunotherapy in a subject comprising administering an **Ig** or **Ig** fusion protein mol. to the subject, the **Ig** mol. having a variable region and a const. region, the **Ig** mol. being modified prior to administration by inactivation of at least a portion of the const. region. The Ig. fusion protein is a IgG, IgM, or IgA which recognizes and binds **Ley** or **Le**. The Ig. fusion protein may also be labeled with radiolabel, enzyme, chromophore, chemiluminescer or fluorescer for tumor diagnosis, or conjugates to cytotoxic agent for cancer therapy. **HBR96**-2B, **hBR96**-2C, **hBR96**-2D, **hBR96**-2E, **hBR96**-2F, **hBR96**-2G, and **hBR96**-2H are provided for the diagnosis and therapy purposes.
IT **203810-39-3 203810-42-8 203810-43-9 203810-44-0 203810-45-1 203810-46-2 203810-47-3 203810-48-4**
RL: PRP (Properties)
(amino acid sequence; **Ig**. fusion protein with mutated const. region for **inhibiting Ig**.-induced **toxicity** in **Ig**. immunotherapy)

L5 ANSWER 2 OF 4 CAPLUS COPYRIGHT 1998 ACS
AN 1995:309167 CAPLUS
DN 122:95959
TI **BR96**-doxorubicin conjugate (BMS-182248) versus doxorubicin: a comparative toxicity assessment in rats
AU Comereski, Charles R.; Peden, W. Michael; Davidson, Thomas J.; Warner, Garvin L.; Hirth, Robert S.; Frantz, Jerry D.
CS Department of Biologics Evaluation, Bristol-Myers Squibb Pharmaceutical Research Institute, Syracuse, NY, 13221-4755, USA
SO Toxicol. Pathol. (1994), 22(5), 473-88
CODEN: TOPADD; ISSN: 0192-6233
DT Journal
LA English
AB The toxicity of BMS-182248, an Ig (cBR96)-cytotoxic drug (doxorubicin) conjugate, was investigated in Sprague-Dawley rats at single i.v. doses of 508, 1,200, and 2,550 mg/m2 (conjugated doxorubicin doses of 14.7, 34.8, and 74 mg/m2, resp.) and compared to that obtained from administration of free doxorubicin at single doses of 33.6 and 72 mg/m2 (approx. equiv. to that contained in the 1,200- and 2,550-mg/m2 doses of BMS-182248, resp.). Necropsies were conducted on day 8, upon death/moribund sacrifice, or after an approx. 3-mo observation period following completion of treatment. Death/moribundity of all rats that received 72 mg/m2 and of 9 of 20 rats given 33.6 mg/m2 free doxorubicin were attributed primarily to delayed cardiotoxicity and glomerulonephropathy. With BMS-182248, death from glomerulonephropathy and cardiotoxicity occurred in only 4 of 20 rats given 2,550 mg/m2 (74 mg/m2 doxorubicin equiv.). No deaths or cardiotoxicity occurred in rats given 508 or 1,200 mg/m2 BMS-182248. Addnl. effects noted with either drug included testicular atrophy, axonal degeneration of sciatic nerve and nerve tracts of brain and spinal cord, teeth (incisor) abnormalities, thymic atrophy, bone marrow hypocellularity, splenic lymphoid and red-pulp depletion, and increased extra-medullary hematopoiesis in the spleen and liver. Also noted were altered chief cells in the stomach, vacuolation of adrenal gland and corpora lutea in the ovary, uterine and seminal vesicle atrophy, ulceration and myocyte regeneration/degeneration in the tongue, increased osteoclasts and osteoblasts in bone, and lymphoid hyperplasia of mandibular lymph node. In general, these effects were more severe in doxorubicin-treated rats. All changes obsd. with BMS-182248 were considered primarily due to the effects of doxorubicin and were substantially less severe (most notably cardiotoxicity) compared to those produced by an equiv. amt. of doxorubicin.

L5 ANSWER 3 OF 4 CAPLUS COPYRIGHT 1998 ACS
AN 1993:624155 CAPLUS
DN 119:224155
TI Phorbol ester, prostaglandin E2, forskolin and okadaic acid differentially modulate interleukin-4-versus interleukin-2-dependent

immunoglobulin induction in human cellular models, in contrast to other selected modifiers of cellular activation

AU Armerding, Dieter; Hren, Andrea

CS Sandoz Forschungsinst., Vienna, Austria

SO Int. Arch. Allergy Immunol. (1993), 101(2), 143-52
CODEN: IAAIEG; ISSN: 1018-2438

DT Journal

LA English

AB Interleukin 2 (IL2) and 4 (IL4) are the most important mediators for Ig synthesis of human B lymphocytes. There is no obvious difference with regard to Ig isotypes induced by either lymphokine except for IgE; only IL4 induces this allergic antibody type. **Monoclonal** anti-CD40 antibodies enhance both IL2- and IL4-dependent Ig induction. Searching for drugs which may inhibit induction of IgE but not of rather non-pathogenic Igs, the authors selected com. compds. which are commonly used as probes for transmembrane signalling pathways in other cellular systems. They included modulators of protein kinase C and intracellular calcium, inducers of cAMP, and inhibitors of protein tyrosine kinase, protein serine/threonine phosphatases and phosphodiesterases. The data presented suggest that IL2- and IL4-mediated B cell activation can be differentially modulated. Phorbol ester at non-cell-**toxic** doses **inhibited** IL4- but not IL2-dependent **Ig** induction. Prostaglandin E2 potently enhanced IgE prodn. stimulated with IL4 alone but was inhibitory in the presence of anti-CD40 as a co-stimulatory signal. IgG1 responses elicited with IL2 plus anti-CD40, in contrast, were not affected. All other compds. did not discriminate between IL2- vs. IL4-mediated Ig induction.

L5 ANSWER 4 OF 4 CAPLUS COPYRIGHT 1998 ACS

AN 1991:119927 CAPLUS

DN 114:119927

TI Mechanism of Staphylococcus aureus exotoxin A inhibition of Ig production by human B cells

AU Moseley, Annemarie B.; Huston, David P.

CS Dep. Med., Baylor Coll. Med., Houston, TX, 77030, USA

SO J. Immunol. (1991), 146(3), 826-32
CODEN: JOIMA3; ISSN: 0022-1767

DT Journal

LA English

AB The effects were examd. of Staphylococcus enterotoxin A (SEA) on proliferation and Ig prodn. of highly purified human B cells. The binding of SEA to MHC class II mols. on B cells does not alter their ability to proliferate in response to S. aureus Cowan strain I (SAC) or to produce Ig in response to SAC plus rIL-2. In contrast, the anti-DR **mAb** L243 inhibited both B cell proliferation and Ig prodn. Unable to det. a direct effect of SEA on B cell function, it was investigated whether the capacity of SEA to inhibit

SAC-induced Ig prodn. by PBMC was T cell-dependent. The results demonstrated that in the presence of T cells, under appropriate conditions, SEA can either function as a nominal antigen for stimulation of B cell proliferation and Ig prodn. or induce T cell-mediated suppression of Ig prodn. SEA-induced Ig prodn. required T cell help, which was dependent on pretreatment of the T cells with irradn. or mitomycin C; Ig prodn. was not induced by SEA in the absence of T cells or in the presence of untreated T cells. Furthermore, SEA inhibited Ig prodn. in SAC-stimulated cultures of autologous B cells and untreated T cells; pretreatment of the T cells with irradn. or mitomycin C abrogated SEA-induced inhibition of Ig prodn. Thus, T cell suppression of SAC-induced Ig prodn. was dependent on T cell proliferation. Similar results were obsd. with both SEA and toxic shock syndrome toxin 1.

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=> d his l6- ful; d 1-32 .bevpat

     FILE 'USPATFULL' ENTERED AT 16:24:45 ON 07 DEC 1998
L6            60 SEA ABB=ON  PLU=ON  L3(S)INHIBIT?
L7            32 SEA ABB=ON  PLU=ON  L6 AND (BR96 OR (BR OR CHIBR OR
                 HBR)(W)96 OR CHIBR96 OR HBR96 OR HB10460 OR HB10036 OR
                 HB(W)(10460 OR 10036) OR MOAB OR MAB OR MONOCLON?)
L8             0 SEA ABB=ON  PLU=ON  L7 AND (LE OR LEY OR LEX)
L9            13 SEA ABB=ON  PLU=ON  L6 AND HYBRIDOMA
L10           32 SEA ABB=ON  PLU=ON  L7 OR L9

L10  ANSWER 1 OF 32  USPATFULL
AN     1998:150943  USPATFULL
TI     Ras farnesyl transferase inhibitors
IN     Marsters, Jr., James C., Oakland, CA, United States
       Brown, Michael S., Dallas, TX, United States
       Crowley, Craig W., Portola Valley, CA, United States
       Goldstein, Joseph L., Dallas, TX, United States
       James, Guy L., Dallas, TX, United States
       McDowell, Robert S., San Francisco, CA, United States
       Oare, David, Belmont, CA, United States
       Rawson, Thomas E., Mountain View, CA, United States
       Reynolds, Mark, South San Francisco, CA, United States
       Somers, Todd C., Foster City, CA, United States
PA     Genentech, Inc., South San Francisco, CA, United States (U.S.
       corporation)
       Board of Regents University of Texas, Austin, TX, United States
       (U.S. corporation)
PI     US 5843941  981201
       WO 9426723  941124
AI     US 94-313068  940926 (8)
       WO 94-US5157  940510
              940926  PCT 371 date
              940926  PCT 102(e) date
                        Searcher  :  Shears   308-4994
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RLI Continuation-in-part of Ser. No. US 93-82202, filed on 24 Jun 1993, now abandoned which is a continuation-in-part of Ser. No. US 93-61961, filed on 14 May 1993, now abandoned
DT Utility
EXNAM Primary Examiner: Bond, Robert T.
LREP Winter, Daryl B.
CLMN Number of Claims: 17
ECL Exemplary Claim: 1,15
DRWN 21 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 8094
AB Benzodiazepine derivatives represented by the structure below are disclosed that act as potent inhibitors of ras farnesyl:protein transferase. Pharmaceutical compositions containing these benzodiazepines are provided for treatment of diseases foe which inhibition of the ras farnesyl:protein transferase as indicated. ##STR1##

INCL INCLM: 514/221.000
INCLS: 540/509.000; 540/514.000
NCL NCLM: 514/221.000
NCLS: 540/509.000; 540/514.000

L10 ANSWER 2 OF 32 USPATFULL
AN 1998:147244 USPATFULL
TI Recombinant lectins
IN Piatak, Jr., Michael, Walnut Creek, CA, United States
PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
PI US 5840522 981124
AI US 95-437048 950509 (8)
RLI Continuation of Ser. No. US 86-837583, filed on 7 Mar 1986, now abandoned which is a continuation-in-part of Ser. No. US 85-715934, filed on 25 Mar 1985, now abandoned which is a continuation-in-part of Ser. No. US 84-653515, filed on 20 Sep 1984, now abandoned
DT Utility
EXNAM Primary Examiner: Degen, Nancy
LREP Marshall, O'Toole et al.; Blackburn, Robert P.
CLMN Number of Claims: 27
ECL Exemplary Claim: 1
DRWN 19 Drawing Figure(s); 19 Drawing Page(s)
LN.CNT 2412
AB DNA sequences encoding full length precursor proteins, which proteins contain both A and B portions of two ricin isotoxins and ricin agglutinin, as well as the linker regions have been determined. These DNAs or portions or modifications thereof are expressed in recombinant hosts to obtain the desired proteins or proteins which can readily converted thereto. One of the ricin isotoxins may be related to ricin E.

INCL INCLM: 435/069.100
INCLS: 435/252.300; 435/252.330; 435/254.200; 435/254.210; 435/320.100; 536/023.600
NCL NCLM: 435/069.100
NCLS: 435/252.300; 435/252.330; 435/254.200; 435/254.210; 435/320.100; 536/023.600

L10 ANSWER 3 OF 32 USPATFULL
AN 1998:79186 USPATFULL
TI Use of quinoline-3-carboxamide compounds for inhibiting the production of tumor necrosis factor (TNF) and/or for the treatment of septic shock
IN Kroemer, Guido Peter, Madrid, Spain
Gonzalo, JoseAngel, Madrid, Spain
Alonso, Carlos Martinez, Madrid, Spain
Kalland, Terje, Loddekopinge, Sweden
PA Pharmacia AB, Stockholm, Sweden (non-U.S. corporation)
PI US 5776947 980707
WO 9503051 950202
AI US 96-586857 960520 (8)
WO 94-SE565 940610
960520 PCT 371 date
960520 PCT 102(e) date
PRAI SE 93-2490 930726
DT Utility
EXNAM Primary Examiner: Goldberg, Jerome D.
LREP Lowe, Price, LeBlanc & Becker
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 535
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The use of a quinoline-3-carboxamide compound comprising structure (I), optionally with substituents for the hydrogen atoms shown (H.sup.1-9), and a salt of compound (I) where (a) ---- represents that there are two conjugated double bonds between the atoms comprised by the dashed line, (b) X.sub.1 and X.sub.2 are separately selected form an oxygen atom or an NH.sup.9 group, said X.sub.1 and X.sub.2 being bound by a single bond to the ring when attached to H.sup.7 or H.sup.8 and by a double bond when not bound to H.sup.7 or H.sup.8, (c) H.sup.1-9 ; are hydrogens with the provision that H.sup.9 is only present when at least one of X.sub.1 and X.sub.2 is the NH.sup.9 group, (d) H.sup.7 and H.sup.8 are hydrogens that are attached to different atoms selected among X.sub.1, X.sub.2 and the nitrogen atom (N) in the quinoline ring, for the manufacture of a composition intended for inhibiting the production of tumor necrosis factor TNF in a living body and/or the treatment of septic shock in a living body.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/312.000
INCLS: 514/313.000
NCL NCLM: 514/312.000
NCLS: 514/313.000

L10 ANSWER 4 OF 32 USPATFULL
AN 1998:28189 USPATFULL
TI Anti-idiotypic antibody composition for inhibiting acute complement-mediated cytotoxicity
IN Koren, Eugen, Oklahoma City, OK, United States
Cooper, David K. C., Oklahoma City, OK, United States
PA Oklahoma Medical Research Foundation, Oklahoma City, OK, United States (U.S. corporation)
Baptist Medical Center of Oklahoma, Inc., Oklahoma City, OK, United States (U.S. corporation)
PI US 5728812 980317
AI US 95-458274 950602 (8)
RLI Division of Ser. No. US 93-133934, filed on 12 Oct 1993, now patented, Pat. No. US 5560911
DT Utility
EXNAM Primary Examiner: Loring, Susan A.
LREP Arnall Golden & Gregory, LLP
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1171
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Antibodies directed against idiotypes on naturally occurring human anti-animal antibodies are disclosed for use in inhibiting xenograft rejection in human patients. An effective quantity of these anti-idiotypic antibodies is injected into the actual or potential xenograft recipient in order to bind to the idiotypes expressed on anti-animal antibodies as well as subpopulations of B lymphocytes, to inhibit hyperacute rejection of transplanted animal tissues or organs by the human patient. Alternatively, anti-idiotypic antibodies are used in the form of immunoaffinity columns to deplete anti-animal antibodies from the recipient's serum. Methods of making mouse **monoclonal**, mouse recombinant, and human recombinant anti-idiotypic antibodies are described, as well as immunoaffinity columns containing immobilized anti-idiotypic antibodies. A method and means for assessing the expected character and severity of a patient's rejection response to transplanted animal tissues is described, as well as methods of identification, isolation and suppression of lymphocytes bearing anti-animal idiotypes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 530/387.200
INCLS: 530/387.100; 530/387.500; 530/391.300; 530/391.100
NCL NCLM: 530/387.200
NCLS: 530/387.100; 530/387.500; 530/391.100; 530/391.300

L10 ANSWER 5 OF 32 USPATFULL
AN 1998:14798 USPATFULL
TI Tricyclic inhibitors of the vitronectin receptor
IN Blackburn, Brent K., San Francisco, CA, United States
Robarge, Kirk, San Francisco, CA, United States
Somers, Todd C., Foster City, CA, United States
PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
PI US 5716951 980210
AI US 95-438143 950508 (8)
RLI Division of Ser. No. US 94-313069, filed on 29 Sep 1994, now patented, Pat. No. US 5602173 And a continuation-in-part of Ser. No. US 93-99019, filed on 29 Jul 1993, now patented, Pat. No. US 5493020
DT Utility
EXNAM Primary Examiner: Bond, Robert T.
LREP Winter, Daryl B.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3731
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A tricylic benzodiazepine derivative that acts as a nonpeptidyl platelet aggregation inhibitor is provided. This inhibitor potently inhibits fibrinogen binding to the GPII.sub.b III.sub.a receptor and is provided in therapeutic compositions for the treatment of diseases for which blocking platelet aggregation is indicated. These nonpeptidyl inhibitors are provided in combination with thrombolytics and anticoagulants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/219.000
INCLS: 514/220.000; 540/497.000; 540/498.000
NCL NCLM: 514/219.000
NCLS: 514/220.000; 540/497.000; 540/498.000

L10 ANSWER 6 OF 32 USPATFULL
AN 1998:11701 USPATFULL
TI IL-4 bone therapy
IN Lewis, David B., Seattle, WA, United States
Perlmutter, Roger M., Seattle, WA, United States
PA Board of Regents of the University of Washington, Seattle, WA, United States (U.S. corporation)
PI US 5714146 980203

AI US 95-418826 950407 (8)
RLI Continuation of Ser. No. US 92-935891, filed on 26 Aug 1992, now abandoned
DT Utility
EXNAM Primary Examiner: Ziska, Suzanne E.
LREP Christensen O'Connor Johnson & Kindness PLLC
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN 11 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 2044
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An in vivo assay for selecting a candidate therapeutic for treating osteoporosis. A candidate reagent is administered to an IL-4 transgenic mammal whose cells contain a recombinant IL-4 coding sequence operably lined to a promoter sequence which is transcriptionally active in bone marrow cells. At the time the candidate reagent is first administered the IL-4 transgenic mammal is either symptomatic of, or asymptomatic of, an osteoporotic phenotype. The candidate reagent is selected as a candidate therapeutic for treating osteoporosis if either amelioration of, or delay in the onset of, the osteoporotic phenotype is observed following administration of the candidate reagent to the IL-4 transgenic mammal.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/130.100
INCLS: 800/002.000; 424/143.100; 424/145.100; 424/152.100; 424/184.100
NCL NCLM: 424/130.100
NCLS: 424/143.100; 424/145.100; 424/152.100; 424/184.100

L10 ANSWER 7 OF 32 USPATFULL
AN 1998:7173 USPATFULL
TI Method of causing selective immunosuppression using HL-60-related lectins
IN Seilhamer, Jeffrey J., 118a Moulton Dr., Milpitas, CA, United States 95035
Nedwin, Glenn, 3245 Oyster Bay Ave., Davis, CA, United States 95616
Bringman, Tim, 817 Santa Florencia, Solana Beach, CA, United States 92075
Couraud, Pierre-Olivier, Auffargis, 9 rue du Perray, 78610 Le Perray, France
PI US 5710257 980120
AI US 96-719551 960925 (8)
RLI Division of Ser. No. US 94-326739, filed on 20 Oct 1994 which is a continuation of Ser. No. US 92-976928, filed on 16 Nov 1992, now abandoned which is a continuation-in-part of Ser. No. US 89-313649, filed on 21 Feb 1989, now abandoned which is a

continuation-in-part of Ser. No. US 88-263734, filed on 28 Oct 1988, now abandoned which is a continuation-in-part of Ser. No. US 88-181747, filed on 14 Apr 1988, now abandoned
DT Utility
EXNAM Primary Examiner: Ziska, Suzanne E.
LREP Morrison & Foerster
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 15 Drawing Figure(s); 13 Drawing Page(s)
LN.CNT 1513
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Pharmaceutical compositions useful in the treatment of autoimmune conditions include as an active ingredient a soluble lectin having a molecular weight of about 14 kilodaltons or a fragment thereof. The lectin or fragment binds .beta.-galactoside-containing moieties independent of the presence or absence of Ca.sup.+2, stimulates hemagglutination of trypsinized rabbit erythrocytes in standard lectin assays wherein the stimulation is inhibited by lactose or thiogalactoside, has an amino acid sequence containing at least one N-glycosylation site and is at least 90% homologous to the amino acid sequence shown in positions 2-135 of FIG. 1 or the relevant portions thereof. The composition is used for treatment of autoimmune conditions such as rheumatoid arthritis, myasthenia gravis, and multiple sclerosis, as well as modulating the immune response in an allergic reactions or to organ or tissue transplant rejection. The inventive composition can be combined with general immunosuppressants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 530/396.000
INCLS: 530/350.000; 435/172.300
NCL NCLM: 530/396.000
NCLS: 530/350.000

L10 ANSWER 8 OF 32 USPATFULL
AN 1998:4562 USPATFULL
TI Methods of using growth inhibitory peptides
IN Mizejewski, Gerald J., Clifton Park, NY, United States
PA Health Research, Incorporated, Albany, NY, United States (U.S. corporation)
PI US 5707963 980113
AI US 96-636386 960423 (8)
RLI Continuation-in-part of Ser. No. US 94-329506, filed on 26 Oct 1994
DT Utility
EXNAM Primary Examiner: Walsh, Stephen; Assistant Examiner: Pak, Michael D.
LREP Jaeckle Fleischmann & Mugel, LLP
CLMN Number of Claims: 12

ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1202
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The subject invention provides non-naturally occurring peptides capable of inhibiting growth factor-stimulated growth of cells. The peptide can be utilized to inhibit growth factor-stimulated growth, such growth factors including, for example, gonadotropins, peptide hormones, synthetic growth factors, and ligands, the ligand having a receptor that is a member of the steroid/thyroid hormone/vitamin receptor superfamily. Also provided are DNA sequences encoding the peptides and methods of producing and using the peptides.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/012.000
INCLS: 435/375.000; 530/324.000
NCL NCLM: 514/012.000
NCLS: 435/375.000; 530/324.000

L10 ANSWER 9 OF 32 USPATFULL
AN 1998:2162 USPATFULL
TI Tricyclic inhibitors of the GPII.sub.b III.sub.a receptor
IN Blackburn, Brent K., San Francisco, CA, United States
Robarge, Kirk, San Francisco, CA, United States
Somers, Todd C., Foster City, CA, United States
PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
PI US 5705890 980106
WO 9504057 950209
AI US 94-313069 940926 (8)
WO 94-US7989 940715
940926 PCT 371 date
940926 PCT 102(e) date
RLI Continuation-in-part of Ser. No. US 93-99019, filed on 29 Jul 1993, now patented, Pat. No. US 5493020, issued on 20 Feb 1996
DT Utility
EXNAM Primary Examiner: Bond, Robert T.
LREP Winter, Daryl B.
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4804
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A tricylic benzodiazepine derivative that acts as a nonpeptidyl platelet aggregation inhibitor is provided. This inhibitor potently inhibits fibrinogen binding to the GPII.sub.b III.sub.a receptor and is provided in therapeutic compositions for the treatment of diseases for which blocking platelet aggregation is

indicated. These nonpeptidyl inhibitors are provided in combination with thrombolytics and anticoagulants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 314/220.000
INCLS: 514/219.000; 540/497.000; 540/498.000
NCL NCLM: 514/220.000
NCLS: 514/219.000; 540/487.000; 540/498.000

L10 ANSWER 10 OF 32 USPATFULL
AN 97:112586 USPATFULL
TI Method of causing selective immunosuppression using HL-60 related lectins
IN Seilhammer, Jeffrey J., Milpitas, CA, United States
Nedwin, Glenn, Davis, CA, United States
Bringman, Tim, Solana Beach, CA, United States
Couraud, Pierre-Olivier, Auffargis, France
PA Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)
PI US 5693760 971202
AI US 94-326739 941020 (8)
RLI Continuation of Ser. No. US 92-976928, filed on 16 Nov 1992, now abandoned which is a continuation-in-part of Ser. No. US 89-313649, filed on 21 Feb 1989, now abandoned which is a continuation-in-part of Ser. No. US 88-263734, filed on 28 Oct 1988, now abandoned which is a continuation-in-part of Ser. No. US 88-181747, filed on 14 Apr 1988, now abandoned
DT Utility
EXNAM Primary Examiner: Ziska, Suzanne E.
LREP Morrison & Foerster
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 15 Drawing Figure(s); 13 Drawing Page(s)
LN.CNT 1533
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Pharmaceutical compositions useful in the treatment of autoimmune conditions include as an active ingredient a soluble lectin having a molecular weight of about 14 kilodaltons or a fragment thereof. The lectin or fragment binds .beta.-galactoside-containing moieties independent of the presence or absence of Ca.sup.+2, stimulates hemagglutination of trypsinized rabbit erythrocytes in standard lectin assays wherein the stimulation is inhibited by lactose or thiogalactoside, has an amino acid sequence containing at least one N-glycosylation site and is at least 90% homologous to the amino acid sequence shown in positions 2-135 of FIG. 1 or the relevant portions thereof. The composition is used for treatment of autoimmune conditions such as rheumatoid arthritis, myasthenia gravis, and multiple sclerosis, as well as modulating the immune response in an allergic reactions or to organ or tissue

transplant rejection. The inventive composition can be combined with general immunosuppressants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 530/396.000
INCLS: 530/350.000; 530/827.000; 435/172.300; 424/278.100
NCL NCLM: 530/396.000
NCLS: 424/278.100; 514/008.000; 530/350.000; 530/827.000

L10 ANSWER 11 OF 32 USPATFULL
AN 97:104105 USPATFULL
TI Epitope-specific **monoclonal** antibodies and immunotoxins and uses thereof
IN Uhr, Jonathan W., Dallas, TX, United States
Vitetta, Ellen S., Dallas, TX, United States
Scheuermann, Richard H., Carrollton, TX, United States
PA Board of Regents, The University of Texas, Austin, TX, United States (U.S. corporation)
PI US 5686072 971111
AI US 94-202042 940222 (8)
RLI Continuation-in-part of Ser. No. US 92-899781, filed on 17 Jun 1992, now abandoned
DT Utility
EXNAM Primary Examiner: Scheiner, Toni R.
LREP Arnold White & Durkee
CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN 12 Drawing Figure(s); 11 Drawing Page(s)
LN.CNT 2395
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The anti-tumor activity of a mixture of anti-CD22 and anti-CD19 immunotoxins is shown to be significantly enhanced in SCID/Daudi mice with disseminated human Daudi lymphoma. Unexpectedly identical enhancement was observed employing a combination of the anti-CD22 immunotoxin with unconjugated anti-CD19 antibodies. Thus combinations of an anti-CD22 immunotoxin and an anti-CD19 immunotoxin or antibody act synergistically and provide advantageous compositions and methods for immunotherapeutic treatment of various diseases including cancer and autoimmune disorders. Also disclosed is data indicating that certain anti-CD19 antibodies alone inhibit proliferation of CD19-positive cells by inducing cell cycle arrest.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/183.100
INCLS: 530/391.700; 530/388.730; 435/007.240
NCL NCLM: 424/183.100
NCLS: 435/007.240; 530/388.730; 530/391.700

L10 ANSWER 12 OF 32 USPATFULL
AN 97:91522 USPATFULL
TI Nonpeptidyl integrin inhibitors having specificity for the GPII.sub.b III.sub.a
IN Blackburn, Brent, San Francisco, CA, United States
Barker, Peter, El Granada, CA, United States
Gadek, Thomas, Oakland, CA, United States
McDowell, Robert, San Francisco, CA, United States
McGee, Lawrence, Pacifica, CA, United States
Somers, Todd, Montara, CA, United States
Webb, Rob, Moss Beach, CA, United States
Robarge, Kirk, San Francisco, CA, United States
PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
PI US 5674865 971007
AI US 95-451794 950526 (8)
RLI Division of Ser. No. US 93-70457, filed on 8 Jun 1993, now abandoned which is a continuation-in-part of Ser. No. US 92-866931, filed on 10 Apr 1992, now patented, Pat. No. US 5250679 which is a continuation-in-part of Ser. No. US 91-781477, filed on 18 Oct 1991, now abandoned
DT Utility
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Wong, King Lit
LREP Winter, Daryl B.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 13454
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A benzodiazepinedione derivative which acts as a nonpeptidyl platelet aggregation inhibitor is provided. This inhibitor potently inhibits fibrinogen binding to the GPII.sub.b III.sub.a receptor and is provided in therapeutic compositions for the treatment of diseases for which blocking platelet aggregation is indicated. These nonpeptidyl inhibitors are provided in combination with thrombolytics and anticoagulants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/213.000
INCLS: 514/215.000; 514/219.000; 514/220.000; 514/221.000; 540/523.000; 540/580.000; 540/593.000; 540/495.000; 540/506.000; 540/490.000; 540/493.000; 540/504.000; 540/512.000
NCL NCLM: 514/213.000
NCLS: 514/215.000; 514/219.000; 514/220.000; 514/221.000; 540/490.000; 540/493.000; 540/495.000; 540/504.000; 540/506.000; 540/512.000; 540/523.000; 540/580.000; 540/593.000

L10 ANSWER 13 OF 32 USPATFULL
AN 97:91520 USPATFULL
TI Nonpeptidyl integrin inhibitors having specificity for the GPII.sub.b III.sub.a receptor
IN Blackburn, Brent, San Francisco, CA, United States
Barker, Peter, El Granada, CA, United States
Gadek, Thomas, Oakland, CA, United States
McDowell, Robert, San Francisco, CA, United States
McGee, Lawrence, Pacifica, CA, United States
Somers, Todd, Montara, CA, United States
Webb, Rob, Moss Beach, CA, United States
Robarge, Kirk, San Francisco, CA, United States
PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
PI US 5674863 971007
AI US 95-451849 950526 (8)
RLI Division of Ser. No. US 93-70457, filed on 8 Jun 1993, now abandoned which is a continuation-in-part of Ser. No. US 92-866931, filed on 10 Apr 1992, now patented, Pat. No. US 5250679 which is a continuation-in-part of Ser. No. US 91-781477, filed on 18 Oct 1991, now abandoned
DT Utility
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Wong, King Lit
LREP Winter, Daryl B.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 13521
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A benzodiazepinedione derivative which acts as a nonpeptidyl platelet aggregation inhibitor is provided. This inhibitor potently inhibits fibrinogen binding to the GPII.sub.b III.sub.a receptor and is provided in therapeutic compositions for the treatment of diseases for which blocking platelet aggregation is indicated. These nonpeptidyl inhibitors are provided in combination with thrombolytics and anticoagulants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/211.000
INCLS: 540/490.000; 540/552.000; 540/523.000; 540/580.000; 540/593.000; 540/495.000; 540/506.000; 540/493.000; 540/504.000; 540/512.000; 514/215.000; 514/219.000; 514/220.000; 514/221.000
NCL NCLM: 514/211.000
NCLS: 514/215.000; 514/219.000; 514/220.000; 514/221.000; 540/490.000; 540/493.000; 540/495.000; 540/504.000; 540/506.000; 540/512.000; 540/523.000; 540/552.000;

540/580.000; 540/593.000

L10 ANSWER 14 OF 32 USPATFULL
AN 97:78435 USPATFULL
TI Nonpeptidyl integrin inhibitors having specificity for the GPII.sub.b III.sub.a receptor
IN Blackburn, Brent, San Francisco, CA, United States
Barker, Peter, El Granada, CA, United States
Gadek, Thomas, Oakland, CA, United States
McDowell, Robert, San Francisco, CA, United States
McGee, Lawrence, Pacifica, CA, United States
Somers, Todd, Montara, CA, United States
Webb, Rob, Moss Beach, CA, United States
Robarge, Kirk, San Franscisco, CA, United States
PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
PI US 5663166 970902
AI US 95-452056 950526 (8)
RLI Division of Ser. No. US 93-70457, filed on 8 Jun 1993, now abandoned which is a continuation-in-part of Ser. No. US 92-866931, filed on 10 Apr 1992, now patented, Pat. No. US 5250679 which is a continuation-in-part of Ser. No. US 91-781477, filed on 18 Oct 1991, now abandoned
DT Utility
EXNAM Primary Examiner: Bond, Robert T.
LREP Winter, Daryl B.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 13432
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A benzodiazepinedione derivative which acts as a nonpeptidyl platelet aggregation inhibitor is provided. This inhibitor potently inhibits fibrinogen binding to the GPII.sub.b III.sub.a receptor and is provided in therapeutic compositions for the treatment of diseases for which blocking platelet aggregation is indicated. These nonpeptidyl inhibitors are provided in combination with thrombolytics and anticoagulants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/213.000
INCLS: 514/215.000; 514/217.000; 540/522.000; 540/523.000; 540/521.000
NCL NCLM: 514/213.000
NCLS: 514/215.000; 514/217.000; 540/521.000; 540/522.000; 540/523.000

L10 ANSWER 15 OF 32 USPATFULL
AN 97:27048 USPATFULL

TI Tripterygium wilfordii hook F extracts and components, and uses thereof

IN Lipsky, Peter E., Dallas, TX, United States
Tao, Xue-Lian, Dallas, TX, United States
Cai, Jian, Dallas, TX, United States
Kovacs, William J., Nashville, TN, United States
Olsen, Nancy J., Nashville, TN, United States
PA Board of Regents, University of TX System, Austin, TX, United States (U.S. corporation)

PI US 5616458 970401
AI US 95-455906 950531 (8)
RLI Continuation-in-part of Ser. No. US 93-168980, filed on 17 Dec 1993 which is a continuation-in-part of Ser. No. US 92-862836, filed on 3 Apr 1992, now patented, Pat. No. US 5294443, issued on 15 Mar 1994 which is a continuation-in-part of Ser. No. US 90-494113, filed on 14 Mar 1990, now abandoned
DT Utility
EXNAM Primary Examiner: Rollins, John W.
LREP Mayfield, Denise L.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN 59 Drawing Figure(s); 25 Drawing Page(s)
LN.CNT 3010
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides for the use of Tripterygium wilfordii Hook F extracts and purified components thereof in the treatment of inflammation or an immune disorder with concomitant lack of steroidal effect. Extracts of this plant (T2) bound to the glucocorticoid receptor and competitively inhibited glucocorticoid mediated cellular processes, such as dexamethasone binding to the glucocorticoid receptor, glucocorticoid mediated activation of target genes, dexamethasone dependent cellular growth, with concomitant inhibition of cyclooxygenase-2 induction and inflammatory processes such as the production of prostaglandin E.sub.2. The T2 extract components triptolide and tripdiolide were effective inhibitors. The particular advantage provided by the methods herein is the treatment or prevention of inflammation and the concomitant lack of steroidal agonist effects and NSAID side effects. Conditions treatable by the present methods include inflammation and immune disorders including autoimmune disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/004.000
INCLS: 435/007.500; 435/007.900; 424/078.050; 424/195.100; 514/469.000; 514/821.000; 514/825.000; 514/886.000
NCL NCLM: 435/004.000
NCLS: 424/078.050; 424/195.100; 435/007.500; 435/007.900; 514/469.000; 514/821.000; 514/825.000; 514/886.000

L10 ANSWER 16 OF 32 USPATFULL
AN 97:1356 USPATFULL
TI Anthrax toxin fusion proteins, nucleic acid encoding same
IN Leppla, Stephen H., Bethesda, MD, United States
Klimpel, Kurt R., Gaithersburg, MD, United States
Arora, Naveen, Delhi, India
Singh, Yogendra, Delhi, India
Nicholls, Peter J., Welling Kent, United Kingdom
PA The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)
PI US 5591631 970107
AI US 93-21601 930212 (8)
DT Utility
EXNAM Primary Examiner: Walsh, Stephen G.
LREP Townsend and Townsend and Crew
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2181
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a nucleic acid encoding a fusion protein, comprising a nucleotide sequence encoding the protective antigen (PA) binding domain of the native lethal factor (LF) protein and a nucleotide sequence encoding an activity inducing domain of a second protein. Also provided is a nucleic acid encoding a fusion protein, comprising a nucleotide sequence encoding the translocation domain and LF binding domain of the native PA protein and a nucleotide sequence encoding a ligand domain which specifically binds a cellular target. Proteins encoded by the nucleic acid of the invention, vectors comprising the nucleic acids and hosts capable of expressing the protein encoded by the nucleic acids are also provided. A composition comprising the PA binding domain of the native LF protein chemically attached to a non-LF activity inducing moiety is further provided. A method for delivering an activity to a cell is provided. The steps of the method include administering to the cell a protein comprising the translocation domain and the LF binding domain of the native PA protein and a ligand domain, and administering to the cell a product comprising the PA binding domain of the native LF protein and a non-LF activity inducing moiety, whereby the product administered is internalized into the cell and performs the activity within the cell.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/252.300
INCLS: 435/320.100; 536/023.400; 536/023.700; 530/350.000; 530/402.000
NCL NCLM: 435/252.300

Searcher : Shears 308-4994

NCLS: 435/320.100; 530/350.000; 530/402.000; 536/023.400; 536/023.700

L10 ANSWER 17 OF 32 USPATFULL
AN 96:111153 USPATFULL
TI Preparations and uses thereof for immunosuppression
IN Lipsky, Peter E., Dallas, TX, United States
Tao, Xue L., Dallas, TX, United States
Cai, Jian, Dallas, TX, United States
PA Board of Regents The University of Texas System, Austin, TX, United States (U.S. corporation)
PI US 5580562 961203
AI US 93-168980 931217 (8)
RLI Continuation-in-part of Ser. No. US 92-862836, filed on 3 Apr 1992, now patented, Pat. No. US 5294443 which is a continuation-in-part of Ser. No. US 90-494113, filed on 14 Mar 1990, now abandoned
DT Utility
EXNAM Primary Examiner: Robinson, Douglas W.; Assistant Examiner: Lee, Howard C.
LREP Akin, Gump, Strauss, Hauer & Feld, L.L.P.
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN 43 Drawing Figure(s); 19 Drawing Page(s)
LN.CNT 2140
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A Tripterygium wilfordii Hook F preparation having an improved LD.sub.50 in mice, an improved therapeutic activity:toxic index ratio and a lower amount of triptolide as compared to previous preparations is disclosed. The LD.sub.50 in mice of the T. wilfordii preparation is greater than about 860 mg/kg, the therapeutic activity:toxic index ratio is greater than about 2.6.times.10.sup.-3, and the amount of triptolide is less than about 1.3 .mu.g/mg. The preparation is useful for immunosuppression, in particular, the suppression of primary antibody response and suppression of autoimmune disease and for the treatment of rheumatoid arthritis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/195.100
INCLS: 514/885.000; 514/908.000; 549/228.000; 549/297.000; 549/298.000
NCL NCLM: 424/195.100
NCLS: 514/885.000; 514/908.000; 549/228.000; 549/297.000; 549/298.000

L10 ANSWER 18 OF 32 USPATFULL
AN 96:94579 USPATFULL
TI Nonpeptidyl integrin inhibitors having specificity for the

GPII.sub.b III.sub.a receptor
IN Blackburn, Brent, San Francisco, CA, United States
Barker, Peter, El Granada, CA, United States
Gadek, Thomas, Oakland, CA, United States
McDowell, Robert, San Francisco, CA, United States
McGee, Lawrence, Pacifica, CA, United States
Somers, Todd, Montara, CA, United States
Webb, Rob, Moss Beach, CA, United States
Robarge, Kirk, San Francisco, CA, United States
PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
PI US 5565449 961015
AI US 95-452479 950526 (8)
RLI Division of Ser. No. US 93-70457, filed on 8 Jun 1993 which is a continuation-in-part of Ser. No. US 92-866931, filed on 10 Apr 1992, now patented, Pat. No. US 5250679 which is a continuation-in-part of Ser. No. US 91-781477, filed on 18 Oct 1991, now abandoned
DT Utility
EXNAM Primary Examiner: Bond, Robert T.
LREP Winter, Daryl B.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1,2
DRWN No Drawings
LN.CNT 13455
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A benzodiazepinedione derivative which acts as a nonpeptidyl platelet aggregation inhibitor is provided. This inhibitor potently inhibits fibrinogen binding to the GPII.sub.b III.sub.a receptor and is provided in therapeutic compositions for the treatment of diseases for which blocking platelet aggregation is indicated. These nonpeptidyl inhibitors are provided in combination with thrombolytics and anticoagulants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/219.000
INCLS: 514/220.000; 514/221.000; 540/493.000; 540/495.000; 540/504.000; 540/512.000
NCL NCLM: 514/219.000
NCLS: 514/220.000; 514/221.000; 540/493.000; 540/495.000; 540/504.000; 540/512.000

L10 ANSWER 19 OF 32 USPATFULL
AN 96:89627 USPATFULL
TI Method of inhibiting acute complement mediated cytotoxicity with anti-idiotypic antibodies
IN Koren, Eugen, Oklahoma City, OK, United States
Cooper, David K. C., Oklahoma City, OK, United States
PA Oklahoma Medical Research Foundation, Oklahoma City, OK, United

States (U.S. corporation)
Integris Baptist Medical Center, Inc., Oklahoma City, OK, United States (U.S. corporation)
PI US 5560911 961001
AI US 93-133934 931012 (8)
DT Utility
EXNAM Primary Examiner: Feisee, Lila; Assistant Examiner: Loring, Susan A.
LREP Arnall Golden & Gregory
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1164
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Antibodies directed against idiotypes on naturally occurring human anti-animal antibodies are disclosed for use in inhibiting xenograft rejection in human patients. An effective quantity of these anti-idiotypic antibodies is injected into the actual or potential xenograft recipient in order to bind to the idiotypes expressed on anti-animal antibodies as well as subpopulations of B lymphocytes, to inhibit hyperacute rejection of transplanted animal tissues or organs by the human patient. Alternatively, anti-idiotypic antibodies are used in the form of immunoaffinity columns to deplete anti-animal antibodies from the recipient's serum. Methods of making mouse **monoclonal**, mouse recombinant, and human recombinant anti-idiotypic antibodies are described, as well as immunoaffinity columns containing immobilized anti-idiotypic antibodies. A method and means for assessing the expected character and severity of a patient's rejection response to transplanted animal tissues is described, as well as methods of identification, isolation and suppression of lymphocytes bearing anti-animal idiotypes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/131.100
INCLS: 424/140.100; 530/387.200
NCL NCLM: 424/131.100
NCLS: 424/140.100; 530/387.200

L10 ANSWER 20 OF 32 USPATFULL
AN 96:23023 USPATFULL
TI Inhibition of IL-2 production by Tripterygium wilfordii Hook F extract
IN Lipsky, Peter E., Dallas, TX, United States
Tao, Xue-Lian, Dallas, TX, United States
PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)
PI US 5500340 960319
AI US 93-136345 931014 (8)

RLI Division of Ser. No. US 92-862836, filed on 3 Apr 1992, now patented, Pat. No. US 5294443, issued on 15 Mar 1994 which is a continuation-in-part of Ser. No. US 90-494113, filed on 14 Mar 1990, now abandoned
DT Utility
EXNAM Primary Examiner: Jones, W. Gary; Assistant Examiner: Myers, Carla
LREP Akin, Gump, Strauss, Hauer & Feld
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN 35 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 1248
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention involves the use of Tripterygium Wilfordii Hook F extracts in the treatment of rheumatoid arthritis. An alcohol extract of this plant (T2) **inhibited** antigen- and mitogen-stimulated proliferation of T cells and B cells, cell cycle progression, interleukin-2 (IL-2) production by T cells, **immunoglobulin** production by B cells and interleukin-2 mRNA production. T2 did not affect IL-2 receptor expression by T cells, IL-1 production by monocytes, the capacity of monocytes to present antigen, or signaling pathways. **Inhibition** could not be accounted for by nonspecific **toxicity**. These results support the conclusion that T2 exerts a powerful suppressive effect on human immune responses. Suppressing autoimmune disease is a most preferred embodiment of this invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/006.000
INCLS: 436/063.000; 935/034.000; 935/077.000
NCL NCLM: 435/006.000
NCLS: 436/063.000

L10 ANSWER 21 OF 32 USPATFULL
AN 96:14918 USPATFULL
TI Tricyclic inhibitors of the GPII.sub.b III.sub.a receptor
IN Blackburn, Brent K., San Francisco, CA, United States
Robarge, Kirk, San Francisco, CA, United States
Somers, Todd C., Montara, CA, United States
PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
PI US 5493020 960220
AI US 93-99019 930729 (8)
DT Utility
EXNAM Primary Examiner: Bond, Robert T.
LREP Winter, Daryl B.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 3570
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A trycylic benzodiazepine derivative which acts as a nonpeptidyl platelet aggregation inhibitor is provided. This inhibitor potently inhibits fibrinogen binding to the GPII.sub.b III.sub.a receptor and is provided in therapeutic compositions for the treatment of diseases for which blocking platelet aggregation is indicated. These nonpeptidyl inhibitors are provided in combination with thrombolytics and anticoagulants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 540/498.000
NCL NCLM: 540/498.000

L10 ANSWER 22 OF 32 USPATFULL
AN 95:29638 USPATFULL
TI Benzazepine platelet aggregation inhibitors having specificity for the GPII.sub.b III.sub.a receptor
IN Blackburn, Brent, San Francisco, CA, United States
McDowell, Robert, San Francisco, CA, United States
Gadek, Thomas, Oakland, CA, United States
Webb, Rob, Moss Beach, CA, United States
PA Genentech, Inc., So. San Francisco, CA, United States (U.S. corporation)
PI US 5403836 950404
AI US 93-58722 930506 (8)
RLI Division of Ser. No. US 92-866931, filed on 10 Apr 1992, now patented, Pat. No. US 5250679 which is a continuation-in-part of Ser. No. US 91-781477, filed on 18 Oct 1991, now abandoned
DT Utility
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Datlow, Philip I.
LREP Winter, Daryl B.
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 11322
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A benzazepine derivative that acts as a nonpeptidyl platelet aggregation inhibitor is provided. This inhibitor potently inhibits fibrinogen binding to the GPII.sub.b III.sub.a receptor and is provided in therapeutic compositions for the treatment of diseases for which blocking platelet aggregation is indicated. These nonpeptidyl inhibitors are provided in combination with thrombolytics and anticoagulants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/213.000
INCLS: 540/495.000; 540/506.000; 540/523.000

NCL NCLM: 514/213.000
NCLS: 540/495.000; 540/506.000; 540/523.000

L10 ANSWER 23 OF 32 USPATFULL
AN 94:22078 USPATFULL
TI Tripterygium wilford II hook f extracts and components thereof for immunosuppression
IN Lipsky, Peter E., Dallas, TX, United States
Tao, Xue-Lian, Dallas, TX, United States
PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)
PI US 5294443 940315
AI US 92-862836 920403 (7)
RLI Continuation-in-part of Ser. No. US 90-494113, filed on 14 Mar 1990, now abandoned
DT Utility
EXNAM Primary Examiner: Rollins, John W.
LREP Arnold, White & Durkee
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 35 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 1210
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention involves the use of Tripterygium Wilfordii Hook F extracts in the treatment of rheumatoid arthritis. An alcohol extract of this plant (T2) **inhibited** antigen- and mitogen-stimulated proliferation of T cells and B cells, cell cycle progression, interleukin-2 (IL-2) production by T cells, **immunoglobulin** production by B cells and interleukin-2 mRNA production. T2 did not affect IL-2 receptor expression by T cells, IL-1 production by monocytes, the capacity of monocytes to present antigen, or signaling pathways. **Inhibition** could not be accounted for by nonspecific **toxicity**. These results support the conclusion that T2 exerts a powerful suppressive effect on human immune responses. Suppressing autoinnune disease is a most preferred embodiment of this invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/195.100
INCLS: 514/885.000
NCL NCLM: 424/195.100
NCLS: 514/885.000

L10 ANSWER 24 OF 32 USPATFULL
AN 94:9659 USPATFULL
TI Method of producing immune response
IN Berzofsky, Jay A., Bethesda, MD, United States
Kawamura, Hajime, Tochigi, Japan

PA The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)
PI US 5283323 940201
AI US 91-715712 910618 (7)
RLI Continuation of Ser. No. US 89-338362, filed on 13 Apr 1989, now abandoned which is a continuation of Ser. No. US 85-763218, filed on 7 Aug 1985, now abandoned
DT Utility
EXNAM Primary Examiner: Hill, Jr., Robert J.; Assistant Examiner: Carlson, K. Cochrane
LREP Birch, Stewart, Kolasch & Birch
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN 14 Drawing Figure(s); 10 Drawing Page(s)
LN.CNT 743
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention discloses a process for enhancing antibody response to an antigen. A novel step in the process is the preparation of a conjugate of the antigen with an anti-immunoglobulin. The conjugate thus prepared is then administered to a host for in vivo effect or presented to T and B cells in a suitable culture system for in vitro response. The present invention by increasing immunogenicity makes it possible to produce antibodies against very low doses of antigens and otherwise weak or insufficient antigens or synthetic vaccines.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 530/387.100
INCLS: 530/387.300; 530/391.700; 424/085.910
NCL NCLM: 424/178.100
NCLS: 424/153.100; 424/173.100; 424/193.100; 530/387.300; 530/388.730; 530/389.600; 530/391.700

L10 ANSWER 25 OF 32 USPATFULL
AN 93:82994 USPATFULL
TI Nonpeptidyl platelet aggregation inhibitors having specificity for the GPII.sub.b III.sub. receptor
IN Blackburn, Brent, San Francisco, CA, United States
McDowell, Robert, San Francisco, CA, United States
Gadek, Thomas, Oakland, CA, United States
Barker, Peter, El Granada, CA, United States
McGee, Lawrence, Pacifica, CA, United States
Webb, Rob, Moss Beach, CA, United States
PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
PI US 5250679 931005
AI US 92-866931 920410 (7)
RLI Continuation-in-part of Ser. No. US 91-781477, filed on 18 Oct

1991, now abandoned
DT Utility
EXNAM Primary Examiner: Bond, Robert T.
LREP Winter, Daryl B.
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 10784
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A benzodiazepinedione derivative which acts as a nonpeptidyl platelet aggregation inhibitor is provided. This inhibitor potently inhibits fibrinogen binding to the GPII.sub.b III.sub.a receptor and is provided in therapeutic compositions for the treatment of diseases for which blocking platelet aggregation is indicated. These nonpeptidyl inhibitors are provided in combination with thrombolytics and anticoagulants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 540/490.000
INCLS: 540/495.000; 540/512.000; 540/523.000
NCL NCLM: 540/490.000
NCLS: 540/495.000; 540/512.000; 540/523.000

L10 ANSWER 26 OF 32 USPATFULL
AN 93:48388 USPATFULL
TI Soluble forms of low affinity Fc gamma receptors, process for their identification and dosage, a corresponding dosage kit, and applications
IN Khayat, David, Paris, France
Unkeless, Jay, Brooklyn, NY, United States
Jacquillat, Claude, Paris, France
PA Universite Pierre et Maire Curie, Paris, France (non-U.S. corporation)
PI US 5219728 930615
WO 8806733 880907
AI US 89-353676 890407 (7)
WO 88-FR103 880223
890407 PCT 371 date
890407 PCT 102(e) date
PRAI FR 87-2400 870224
DT Utility
EXNAM Primary Examiner: Nucker, Christine M.; Assistant Examiner: Preston, David R.
LREP Jacobson, Price, Holman & Stern
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 8 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 601
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Receptors, characterized by the fact that they consist of the product obtained by affinity chromatography on a column coupled with 3 G8 antibodies or lectins or polyclonal anti-receptor FcR antibodies of a biological fluid of human origin, then by gel permeation. The spectrum of said product, electrophoresis acrylamide gel in reducing condition, comprising a major band corresponding to a molecular mass of between 72000 and 76000 daltons, and a number of minor bands. According to its purified form, the receptor consists of a glycoprotein with a molecular mass of between 72000 and 76000 daltons, recognized by ELISA and Western Blotting by the **monoclonal** anti-Leu 11b antibody. Application of said receptors to diagnosis and to follow-up treatment of diseases involving Fc receptors (infectious diseases, diseases of the autoimmune system, rejection of transplants, cancer and myeloma and AIDS), as well as to the study of human polymorphisms.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/007.200
INCLS: 530/380.000; 530/395.000; 435/007.900; 435/007.920; 435/007.940; 435/007.950; 514/002.000; 514/008.000
NCL NCLM: 435/007.200
NCLS: 435/007.900; 435/007.920; 435/007.940; 435/007.950; 514/002.000; 514/008.000; 530/380.000; 530/395.000

L10 ANSWER 27 OF 32 USPATFULL
AN 91:71212 USPATFULL
TI Methods for screening antibodies for use as immunotoxins
IN Uhr, Jonathan W., 12355 Montego Plz., Dallas, TX, United States 75230
Vitetta, Ellen S., 6914 Pemberton Dr., Dallas, TX, United States 75230
PA Board of Regents, Austin, TX, United States (U.S. corporation)
PI US 5045451 910903
AI US 88-262974 881026 (7)
DT Utility
EXNAM Primary Examiner: Saunders, David A.
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 671
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present disclosure described an assay for screening **monoclonal** antibodies for their potential as highly cytotoxic immunotoxins. The assay involves treating cells with dilutions of the test antibody followed by a Fab fragment of a secondary antibody coupled to an A chain toxin ("indirect assay"). The cytotoxicity of the indirect assay is compared to that of the direct assay where the **monoclonal** antibody is coupled to

an A chain toxin. Indirect and direct assays were carried out using 14 antibodies and a panel of 8 human and mouse cell types. The two assays showed virtually 100% correlation. The indirect assay, therefore, predicts the potency of a given **monoclonal** antibody to make an effective immunotoxin and should be useful in screening **monoclonal** antibodies for use as immunotoxins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/007.230
INCLS: 435/029.000; 435/007.240; 436/503.000; 436/512.000; 436/519.000; 436/547.000; 436/548.000; 436/813.000
NCL NCLM: 435/007.230
NCLS: 435/007.240; 435/029.000; 436/503.000; 436/512.000; 436/519.000; 436/547.000; 436/548.000; 436/813.000

L10 ANSWER 28 OF 32 USPATFULL
AN 90:61235 USPATFULL
TI Hepatic blocking agents
IN Baldwin, Robert W., Long Eaton, England
Byers, Vera S., San Francisco, CA, United States
PA Xoma Corporation, Berkeley, CA, United States (U.S. corporation)
PI US 4946675 900807
AI US 87-55266 870527 (7)
DT Utility
EXNAM Primary Examiner: Draper, Garnette
LREP Townsend and Townsend
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 607
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel methods and compositions are provided for the enhancement of the biodistribution of immunoconjugates useful in the diagnosis and treatment of a variety of conditions including cancer in many of its forms. The compositions of the present invention provide for enhanced bioavailability of immunoconjugates for the most part by blocking mammalian cell surface receptors present on cells of the reticuloendothelial system, especially in tissues responsible for the elimination of waste products and blood filtration. Such tissues include the liver, spleen, and kidneys. The compositions are administered in conjunction with an immunoconjugate in a pharmaceutically acceptable vehicle and may be provided in kits for convenient administration.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/085.910
INCLS: 514/002.000; 514/008.000; 514/023.000; 514/059.000; 514/885.000; 530/389.000; 530/391.000; 435/007.000;

435/810.000; 436/543.000
NCL NCLM: 424/182.100
NCLS: 435/007.230; 435/810.000; 436/543.000; 514/002.000; 514/008.000; 514/023.000; 514/059.000; 514/885.000; 530/391.700; 530/391.900

L10 ANSWER 29 OF 32 USPATFULL
AN 89:15167 USPATFULL
TI Stable formulations of ricin toxin a chain and of RTA-immunoconjugates and stabilizer screening methods therefor
IN Ferris, Robert, Walnut Creek, CA, United States
PA Cetus Corporation, Emeryville, CA, United States (U.S. corporation)
PI US 4808705 890228
AI US 86-944347 861219 (6)
DT Utility
EXNAM Primary Examiner: Phillips, Delbert R.; Assistant Examiner: Draper, Garnette D.
LREP Lauder, Leona L.; Halluin, Albert P.; Giotta, Gregory J.
CLMN Number of Claims: 46
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 937
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Highly stable pharmaceutical compositions suitable for parenteral administration to animals or humans comprising a therapeutically effective amount of an RTA-immunoconjugate dissolved in an inert carrier method comprising a stabilizer are claimed. Screening methods for selecting stabilizers effective in preventing precipitation and aggregation of such compositions are described. Preferred stabilizers includes glycerol at a concentration (v/v) of from about 25 to about 35%; dextran sulfates having molecular weights from about 0.1.times.10.sup.6 to about 2.times.10.sup.6 daltons; and human serum albumin.

The invention further comprises such compositions which have been lyophilized and/or reconstituted wherein the stabilizer is non-volatile, and may further comprise a carbohydrate stabilizer.

The invention further comprises stabilized RTA compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 530/391.000
INCLS: 530/390.000; 530/808.000; 530/370.000; 424/085.910; 514/002.000; 514/885.000; 514/008.000
NCL NCLM: 424/183.100
NCLS: 424/278.100; 514/002.000; 514/008.000; 514/885.000; 530/370.000; 530/391.700; 530/808.000; 530/861.000

L10 ANSWER 30 OF 32 USPATFULL
AN 88:82113 USPATFULL
TI Anti-immunoglobulin toxin conjugates useful in the treatment of B cell tumors
IN Uhr, Jonathan W., Dallas, TX, United States
Vitetta, Ellen S., Dallas, TX, United States
PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)
PI US 4792447 881220
AI US 83-498754 830527 (6)
RLI Continuation-in-part of Ser. No. US 81-286090, filed on 23 Jul 1981, now abandoned
DT Utility
EXNAM Primary Examiner: Hazel, Blondel
LREP Arnold, White & Durkee
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 893
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Highly specific antibodies directed against immunoglobulin determinants coupled to one or more toxin molecules provide antibody-toxin conjugates which are useful in selectively inhibiting the growth of target immunoglobulin generating cells. The antibody-toxin conjugate consists of an antibody specific for a selected immunoglobulin determinant including isotypic, allotypic or idiotypic variable determinants, coupled to one or more toxin molecules. Anti-idiotype toxin conjugates are provided which have specificity which distinguishes B cell tumor cells from normal B cells. Also disclosed is an antibody-toxin conjugate consisting of anti-IgD A chain. The antibody-toxin conjugate is used as a cell or tumor specific cytotoxic agent directed selectively against those cells expressing the corresponding immunoglobulin to which the antibody portion has specificity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/085.910
INCLS: 530/387.000
NCL NCLM: 424/183.100
NCLS: 424/805.000; 424/809.000; 530/387.200; 530/388.730; 530/391.700; 530/862.000; 530/864.000; 530/866.000

L10 ANSWER 31 OF 32 USPATFULL
AN 83:1740 USPATFULL
TI Protein hybrid having cytotoxicity and process for the preparation thereof
IN Masuho, Yasuhiko, Hino, Japan
Hara, Takeshi, Hachioji, Japan
PA Teijin Limited, Osaka, Japan (non-U.S. corporation)

PI US 4368149 830111
AI US 81-331342 811216 (6)
PRAI JP 80-180553 801222
DT Utility
EXNAM Primary Examiner: Schain, Howard E.
LREP Sughrue, Mion, Zinn, Macpeak & Seas
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 689
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A protein hybrid having cytotoxicity obtained by covalently bonding an immunoglobulin or its fragment, which is capable of binding selectively to an antigen possessed by a cell to be destroyed, to a protein, which is obtained from Momordica charantia and has an activity to terminate protein synthesis. This protein hybrid displays remarkable cytotoxicity against targel cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 260/112.000B
INCLS: 424/085.000; 424/088.000
NCL NCLM: 530/391.900
NCLS: 424/179.100; 424/184.100; 530/389.600; 530/391.700; 530/866.000

L10 ANSWER 32 OF 32 USPATFULL
AN 82:60306 USPATFULL
TI Cytotoxic protein hybrid and process for the preparation thereof
IN Masuho, Yasuhiko, Hino, Japan
Kishida, Kazuo, Hino, Japan
Hara, Takeshi, Hachioji, Japan
PA Teijin Limited, Osaka, Japan (non-U.S. corporation)
PI US 4363758 821214
AI US 81-331347 811216 (6)
PRAI JP 80-180552 801222
DT Utility
EXNAM Primary Examiner: Schain, Howard E.
LREP Sughrue, Mion, Zinn, Macpeak & Seas
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 693
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A cytotoxic protein hybrid obtained by covalently bonding an immunoglobulin or its fragment, which is capable of linking selectively with an antigen possessed by a cell to be destroyed, to a protein, which is obtained from Phytolacca americana and has an activity to terminate protein synthesis. This protein hybrid

displays remarkable cytotoxicity against target cells.

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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL    INCLM: 260/112.000B
        INCLS: 424/085.000; 424/088.000
NCL     NCLM:  530/391.900
        NCLS:  424/179.100; 424/183.100; 530/370.000; 530/379.000;
               530/389.600; 530/391.700; 530/866.000

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L1          3645 SEA FILE=REGISTRY ABB=ON  PLU=ON  IMMUNOGLOBULIN ?/CN
L11       115196 SEA FILE=CAPLUS ABB=ON  PLU=ON  L1 OR IMMUNOGLOBULIN OR
                 IMMUNO GLOBULIN OR IG#
L12          459 SEA FILE=CAPLUS ABB=ON  PLU=ON  L11(S)TOXIC?
L13           43 SEA FILE=CAPLUS ABB=ON  PLU=ON  L12(S)INHIBIT?
L14            7 SEA FILE=CAPLUS ABB=ON  PLU=ON  L13 AND (LEX OR LEY OR
                 LE OR BR96 OR (BR OR CHIBR OR HBR)(W)96 OR CHIBR96 OR
                 HBR96 OR HB10460 OR HB10036 OR HB(W)(10460 OR 10036) OR
                 MOAB OR MAB OR MONOCLON? OR HYBRIDOMA)

=> s l14 not l5

L15            3 L14 NOT L5

=> d 1-3 .bevstr
```

L15 ANSWER 1 OF 3 CAPLUS COPYRIGHT 1998 ACS
AN 1992:649799 CAPLUS
DN 117:249799
TI Selection of an escape variant of Borrelia burgdorferi by use of bactericidal **monoclonal** antibodies to OspB
AU Coleman, James L.; Rogers, Rene C.; Benach, Jorge L.
CS State of New York Dep. Health, Stony Brook, NY, 11794-8692, USA
SO Infect. Immun. (1992), 60(8), 3098-104
CODEN: INFIBR; ISSN: 0019-9567
DT Journal
LA English
AB Two IgG **monoclonal** antibodies (**MAbs**) to outer surface protein B (OspB) (CB2 and CB6), affinity purified from mouse ascitic fluid, exhibited concn.-dependent inhibitory and bactericidal properties against B. burgdorferi after a 24-h incubation period in spirochete medium. Fab fragments derived from these **MAbs** showed the same effects, indicating that they were not caused by agglutination of the organisms by the intact **MAbs**. The inhibition of spirochete growth in cultures contg. **MAbs** was also detected by spectrophotometric anal. of the media. CB2 did not inhibit the growth of B. hermsii or the BEP4 strain of B. burgdorferi, neither of which is recognized by the **MAb**. Affinity-purified **IgG** from **hybridoma** supernatants had similar effects on B. burgdorferi as the ascitic-fluid-derived **IgG** did, indicating that the **inhibitory** and bactericidal properties were not due to nonspecific **toxic** contaminants. The bactericidal properties of the **MAbs** were not complement-dependent. SDS-PAGE anal. of B. burgdorferi organisms surviving after exposure to CB2 revealed an escape variant which failed to express OspB. The continued presence of OspA in these escape variants indicates that the lack of OspB was not due to the loss of the plasmid which contains the genes for both of these proteins.

L15 ANSWER 2 OF 3 CAPLUS COPYRIGHT 1998 ACS
AN 1992:542983 CAPLUS
DN 117:142983
TI **Inhibition** of hematopoietic tumor growth by combined treatment with deferoxamine and an **IgG monoclonal** antibody against the transferrin receptor: evidence for a threshold model of iron deprivation **toxicity**
AU Kemp, John D.; Thorson, John A.; Stewart, Barbara C.; Naumann, Paul W.
CS Coll. Med., Univ. Iowa, Iowa City, IA, 52242, USA
SO Cancer Res. (1992), 52(15), 4144-8
CODEN: CNREA8; ISSN: 0008-5472
DT Journal

LA English
AB Recent studies have suggested that iron deprivation may represent a useful new approach in cancer therapy, and several strategies for producing such deprivation are now under investigation. The authors recently provided evidence that combined treatment with the iron chelator deferoxamine and an IgG **monoclonal** antibody against the transferrin receptor (ATRA) produces synergistic inhibition of hematopoietic tumor cell growth in vitro (J. D. Kemp, K. M. Smith, L. J. Kanner et al., 1900). The current study is an attempt to analyze the mechanisms responsible for the synergistic interaction. The data show that a single IgG ATRA can produce up to 75% inhibition of iron uptake while having little effect on DNA synthesis; this suggests that tumor cells either take up or have stored amts. of iron well in excess of that required to support immediate metabolic needs. When deferoxamine and the IgG ATRA are used together, the effects on iron acquisition and receptor down-modulation are either additive or subadditive but are clearly not synergistic. Overall, the findings suggest that the IgG ATRA produces an injury to iron uptake that is just below a crit. threshold and that the addnl. effect provided by the iron chelator is sufficient to exceed that threshold and produce a rapid depletion of iron pools that are vital for short-term DAN synthesis. IgG ATRAS thus seem to be of even greater interest as therapeutic reagents, and further study of their properties and of how they interact with deferoxamine appears to be warranted.

L15 ANSWER 3 OF 3 CAPLUS COPYRIGHT 1998 ACS
AN 1983:105510 CAPLUS
DN 98:105510
TI **Monoclonal** antibody and an antibody-toxin conjugate to a cell surface proteoglycan of melanoma cells suppress in vivo tumor growth
AU Bumol, T. F.; Wang, Q. C.; Reisfeld, R. A.; Kaplan, N. O.
CS Dep. Immunol., Scripps Clin. Res. Found., La Jolla, CA, 92037, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1983), 80(2), 529-33
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB A **monoclonal** antibody directed against a cell surface chondroitin sulfate proteoglycan of human melanoma cells, 9.2.27, and its diphtheria toxin A chain (DTA) conjugate were investigated for their effects on in vitro protein synthesis and in vivo tumor growth of human melanoma cells. The 9.2.27 **IgG** and its DTA conjugate display similar serol. activities against melanoma target cells but only the conjugate can induce consistent in vitro **inhibition** of protein synthesis and **toxicity** in M21 melanoma cells. However, both 9.2.27 IgG and its DTA conjugate induce suppression of M21 tumor growth in vivo in an immunotherapy model of a rapidly growing tumor in athymic nu/nu mice, suggesting

that other host mechanisms may mediate **monoclonal** antibody-induced tumor suppression.

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=> d his l20-; d 1-21 .bevpat

     (FILE 'USPATFULL' ENTERED AT 16:31:58 ON 07 DEC 1998)
L16          93 S L14
L17          12 S L16 AND FUS? PROTEIN
L18          83 S L16 AND ADMIN?
L20         135 S L13
L21          92 S L20 AND (BR96 OR (BR OR CHIBR OR HBR)(W)96 OR CHIBR96 OR
                HBR)(W)96 OR CHIBR96 OR HBR96 OR HB10460 OR HB10036 OR
                HB(W)(10460 OR 10036) OR MOAB OR MAB OR MONOCLON? OR
                HYBRIDOMA)
L22           1 S L21 AND (LEY OR LEX OR LE)
L23          27 S L18 AND (IMMUNOTHERAP? OR IMMUN? THERAP?)
L24          21 S (L22 OR L23) NOT L10

L24  ANSWER 1 OF 21  USPATFULL
AN     1998:128265  USPATFULL
TI     Substituted amino alcohol compounds
IN     Klein, J. Peter, Vashon, WA, United States
       Underiner, Gail E., Brier, WA, United States
       Kumar, Anil M., Seattle, WA, United States
PA     Cell Therapeutics, Inc., Seattle, WA, United States (U.S.
       corporation)
PI     US 5824677  981020
AI     US 95-474816  950607 (8)
RLI    Division of Ser. No. US 94-303842, filed on 8 Sep 1994, now
       patented, Pat. No. US 5641783 which is a continuation-in-part of
       Ser. No. US 93-152650, filed on 12 Nov 1993, now patented, Pat.
       No. US 5801181 And Ser. No. US 93-164081, filed on 8 Dec 1993, now
       patented, Pat. No. US 5470878 , said Ser. No. US   -152650 And
       Ser. No. US   -164081 , each Ser. No. US   - which is a
       continuation-in-part of Ser. No. US 93-40820, filed on 31 Mar
       1993, now abandoned
DT     Utility
EXNAM  Primary Examiner: Raymond, Richard L.; Assistant Examiner:
       Cebulak, Mary C.
LREP   McDermott, Will & Emery; Faciszewski, Esq., Stephen
CLMN   Number of Claims: 18
ECL    Exemplary Claim: 1
DRWN   120 Drawing Figure(s); 89 Drawing Page(s)
LN.CNT 3136
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB     Disclosed are compounds having a straight or branched aliphatic
       hydrocarbon structure of formula I: ##STR1## In formula I, n is an
       integer from one to four and m is an integer from four to twenty.
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Independently, R.sub.1 and R.sub.2 are hydrogen, a straight or branched chain alkyl, alkenyl or alkynyl of up to twenty carbon atoms in length or --(CH.sub.2).sub.w R.sub.5. If R.sub.1 or R.sub.2 is --(CH.sub.2).sub.w R.sub.5, w may be an integer from one to twenty and R.sub.5 may be an hydroxyl, halo, C.sub.1-8 alkoxyl group or a substituted or unsubstituted carbocycle or heterocycle. Alternatively, R.sub.1 and R.sub.2 may jointly form a substituted or unsubstituted, saturated or unsaturated heterocycle having from four to eight carbon atoms, N being a hetero atom of the resulting heterocyle. R.sub.3 may be either hydrogen or C.sub.13. In the compounds, a total sum of carbon atoms comprising R.sub.1 or R.sub.2, (CH.sub.2).sub.n and (CH.sub.2).sub.m does not exceed forty. R.sub.4 is a hetorocycle comprising a substituted or unsubstituted, oxidized or reduced ring system, the ring system having a single ring or two to three fused rings, a ring comprising from three to seven ring atoms. The disclosed compounds are effective agents to inhibit undesirable responses to cell stimuli.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 514/222.500

INCLS: 514/223.500; 514/224.500; 514/226.800; 514/227.500; 514/228.800; 514/229.200; 514/230.500; 514/230.800; 514/237.800; 514/248.000; 514/249.000; 514/255.000; 514/258.000; 514/274.000; 514/301.000; 514/303.000; 514/311.000; 514/351.000; 514/360.000; 514/361.000; 514/362.000; 514/363.000; 514/364.000; 514/365.000; 514/367.000; 514/372.000; 514/373.000; 514/374.000; 514/375.000; 514/376.000; 514/378.000; 514/379.000; 514/380.000; 514/387.000; 514/395.000; 514/415.000; 514/418.000; 514/424.000; 514/425.000; 514/433.000; 514/452.000; 514/432.000; 514/438.000; 346/113.000; 346/114.000; 346/164.000; 346/300.000; 549/014.000; 549/050.000; 549/075.000; 549/367.000; 549/368.000; 544/002.000; 544/003.000; 544/005.000; 544/008.000; 544/053.000; 544/063.000; 544/065.000; 544/066.000; 544/067.000; 544/090.000; 544/091.000; 544/127.000; 544/128.000; 544/162.000; 544/215.000; 544/219.000; 544/229.000; 544/235.000; 544/237.000; 544/255.000; 544/278.000; 544/311.000; 544/353.000; 544/385.000; 548/123.000; 548/125.000; 548/131.000; 548/134.000; 548/143.000; 548/146.000; 548/153.000; 548/174.000; 548/207.000; 548/214.000; 548/215.000; 548/217.000; 548/221.000; 548/228.000; 548/229.000; 548/237.000; 548/240.000; 548/241.000; 548/243.000; 548/247.000; 548/267.200; 548/303.700; 548/307.100; 548/453.000; 548/486.000; 548/543.000; 548/546.000

NCL NCLM: 514/222.500

NCLS: 514/223.500; 514/224.500; 514/226.800; 514/227.500;

514/228.800; 514/229.200; 514/230.500; 514/230.800;
514/237.800; 514/248.000; 514/249.000; 514/255.000;
514/258.000; 514/274.000; 514/301.000; 514/303.000;
514/311.000; 514/351.000; 514/360.000; 514/361.000;
514/362.000; 514/363.000; 514/364.000; 514/365.000;
514/367.000; 514/372.000; 514/373.000; 514/374.000;
514/375.000; 514/376.000; 514/378.000; 514/379.000;
514/380.000; 514/387.000; 514/395.000; 514/415.000;
514/418.000; 514/424.000; 514/425.000; 514/432.000;
514/433.000; 514/438.000; 514/452.000; 544/002.000;
544/003.000; 544/005.000; 544/008.000; 544/053.000;
544/063.000; 544/065.000; 544/066.000; 544/067.000;
544/090.000; 544/091.000; 544/127.000; 544/128.000;
544/162.000; 544/215.000; 544/219.000; 544/229.000;
544/235.000; 544/237.000; 544/255.000; 544/278.000;
544/311.000; 544/353.000; 544/385.000; 546/113.000;
546/114.000; 546/164.000; 546/300.000; 548/123.000;
548/125.000; 548/131.000; 548/134.000; 548/143.000;
548/146.000; 548/153.000; 548/174.000; 548/207.000;
548/214.000; 548/215.000; 548/217.000; 548/221.000;
548/228.000; 548/229.000; 548/237.000; 548/240.000;
548/241.000; 548/243.000; 548/247.000; 548/267.200;
548/303.700; 548/307.100; 548/453.000; 548/486.000;
548/543.000; 548/546.000; 549/014.000; 549/050.000;
549/075.000; 549/367.000; 549/368.000

L24 ANSWER 2 OF 21 USPATFULL
AN 1998:128236 USPATFULL
TI Rnase-cv (coriolus versicolor)
IN Yang, Mable M. P., Block, 17B, fourth Fl., Baguio Villa, Hong Kong
Chen, George, Block, 17B, fourth Fl., Baguio Villa, Hong Kong
PI US 5824648 981020
AI US 94-359222 941219 (8)
RLI Continuation-in-part of Ser. No. US 92-983238, filed on 30 Nov 1992, now patented, Pat. No. US 5374714
DT Utility
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Mohamed, Abdel A.
LREP Norris, Jerome J.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 26 Drawing Figure(s); 17 Drawing Page(s)
LN.CNT 797
AB A method of obtaining a novel polypeptide from a crude extraction product of polysaccharide peptide Coriolus versicolor comprising: a) boiling a water soluble powder of polysaccharide peptide Coriolus versicolor; b) centrifuging a boiled product from step a); c) filtering a centrifuged product from step b); d) purifying a solution from step c) by gel filtration chromatography; e)

subjecting the purified material from step d) to HPLC using a reversed-phase at ambient temperature, f) subjecting the purified material from step e) to capillary isoelectrophoresis focusing; g) further purifying this product by HPLC and ionic exchange columns and h) purifying a protein by SDS-PAGE and i) recovering a peptide from 12 Kd to 16 kD. The peptide has the partial amino acid sequence GTAAAKEFERQHM SEQ ID NO:1.

INCL INCLM: 514/014.000
INCLS: 514/008.000; 514/012.000; 530/322.000; 530/324.000; 530/327.000; 530/350.000; 530/371.000; 530/395.000; 530/523.000; 536/123.100
NCL NCLM: 514/014.000
NCLS: 514/008.000; 514/012.000; 530/322.000; 530/324.000; 530/327.000; 530/350.000; 530/371.000; 530/395.000; 530/823.000; 536/123.100

L24 ANSWER 3 OF 21 USPATFULL
AN 1998:95236 USPATFULL
TI Mutant diphtheria toxin conjugates
IN Johnson, Virginia G., College Park, MD, United States
Greenfield, Larry, Emeryville, CA, United States
Youle, Richard J., Garrett Park, MD, United States
Laird, Walter, Pinole, CA, United States
PA The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)
Cetus Corporation, Emeryville, CA, United States (U.S. corporation)
PI US 5792458 980811
AI US 94-323591 941017 (8)
RLI Continuation of Ser. No. US 92-934250, filed on 25 Aug 1992, now abandoned which is a division of Ser. No. US 89-301376, filed on 25 Jan 1989, now patented, Pat. No. US 5208021 which is a division of Ser. No. US 88-236225, filed on 25 Aug 1988, now abandoned which is a continuation-in-part of Ser. No. US 87-105172, filed on 5 Oct 1987, now abandoned
DT Utility
EXNAM Primary Examiner: Scheiner, Toni R.; Assistant Examiner: Lucas, John
LREP Klarquist Sparkman Campbell Leigh & Whinston
CLMN Number of Claims: 39
ECL Exemplary Claim: 1
DRWN 14 Drawing Figure(s); 9 Drawing Page(s)
LN.CNT 1444
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A potent and specific immunotoxin is prepared by coupling an inactivated diphtheria toxin to a binding moiety such as a **monoclonal** antibody or transferrin. The immunotoxins are

specific for human tumors and leukemias and are indistinguishable in cell toxicity from that of the native toxin linked to the binding domain without the toxicity to other cells. The immunotoxin is useful in treating graft versus host disease as well as selectively killing tumor cells, such as medulloblastoma and glioblastoma cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/183.100
INCLS: 424/155.100; 424/174.100; 424/094.100; 424/832.000; 514/012.000; 530/350.000; 530/387.700; 530/391.700
NCL NCLM: 424/183.100
NCLS: 424/094.100; 424/155.100; 424/174.100; 424/832.000; 514/012.000; 530/350.000; 530/387.700; 530/391.700

L24 ANSWER 4 OF 21 USPATFULL
AN 1998:91837 USPATFULL
TI Polyclonal antibody libraries
IN Sharon, Jacqueline, Chestnut Hill, MA, United States
PA The Trustees of Boston University, Boston, MA, United States (U.S. corporation)
PI US 5789208 980804
AI US 97-802824 970219 (8)
RLI Continuation of Ser. No. US 94-189360, filed on 31 Jan 1994, now abandoned
DT Utility
EXNAM Primary Examiner: Chambers, Jasemine C.; Assistant Examiner: Priebe, Scott D.
LREP Eisenstein, Ronald I.
CLMN Number of Claims: 26
ECL Exemplary Claim: 1
DRWN 21 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 2370
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention is directed to methods for the creation and use of libraries of proteins which comprise polyclonal antibodies to a common antigen or group of antigens, receptor proteins with related variable regions, or other immune related proteins with variable regions. These polyclonal antibody libraries can be used to treat or prevent diseases and disorders including neoplasia such as cancer and other malignancies, parasitic infections, bacterial infections, viral infections and disorders such as genetic defects and deficiencies. Protein libraries may be patient-specific, disease-specific or both patient- and disease-specific. Libraries can also be used to detect a disease or disorder in a patient either by direct imaging or through the use of a diagnostic kit. The invention further includes novel cloning methods for the creation and transfer of nucleic acid sequences encoding protein variable regions and novel cloning

vectors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/091.410
INCLS: 435/006.000; 435/006.910; 435/091.400; 435/172.000; 435/320.100
NCL NCLM: 435/091.410
NCLS: 435/006.000; 435/069.100; 435/091.400; 435/320.100; 435/488.000; 435/489.000

L24 ANSWER 5 OF 21 USPATFULL
AN 1998:79344 USPATFULL
TI Method for preparing substituted amino alcohol compounds
IN Klein, J. Peter, Vashon, WA, United States
Underiner, Gail E., Brier, WA, United States
Kumar, Anil M., Seattle, WA, United States
PA Cell Therapeutics, Inc., Seattle, WA, United States (U.S. corporation)
PI US 5777117 980707
AI US 95-472569 950607 (8)
RLI Division of Ser. No. US 94-303842, filed on 8 Sep 1994 which is a continuation-in-part of Ser. No. US 93-152650, filed on 12 Nov 1993 And Ser. No. US 93-164081, filed on 8 Dec 1993 which is a continuation-in-part of Ser. No. US 93-40820, filed on 31 Mar 1993, now abandoned , said Ser. No. US -152650 which is a continuation-in-part of Ser. No. US -40820
DT Utility
EXNAM Primary Examiner: Dees, Jose G.; Assistant Examiner: Cebulak, Mary C.
LREP McDermott, Will & Emery
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN 118 Drawing Figure(s); 92 Drawing Page(s)
LN.CNT 3153
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed is a process for preparing compounds having a straight or branched aliphatic hydrocarbon structure of formula I: ##STR1## In formula I, n is an integer from one to four and m is an integer from four to twenty. Independently, R.sub.1 and R.sub.2 are hydrogen, a straight or branched chain alkyl, alkenyl or alkynyl of up to twenty carbon atoms in length or --(CH.sub.2).sub.w R.sub.5. If R.sub.1 or R.sub.2 is --(CH.sub.2).sub.w R.sub.5, w may be an integer from one to twenty and R.sub.5 may be an hydroxyl, halo, C.sub.1-8 alkoxyl group or a substituted or unsubstituted carbocycle or heterocycle. Alternatively, R.sub.1 and R.sub.2 may jointly form a substituted or unsubstituted, saturated or unsaturated heterocycle having from four to eight carbon atoms, N being a hetero atom of the resulting heterocyle. R.sub.3 may be either hydrogen or C.sub.1-3. In the compounds, a

total sum of carbon atoms comprising R.sub.1 or R.sub.2, (CH.sub.2).sub.n and (CH.sub.2).sub.m does not exceed forty. R.sub.4 is a terminal moiety comprising a substituted or unsubstituted, oxidized or reduced ring system, the ring system having a single ring or two to three fused rings, a ring comprising from three to seven ring atoms. The disclosed compounds are effective agents to inhibit undesirable responses to cell stimuli.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 544/267.000
INCLS: 544/257.000; 544/285.000; 544/286.000; 544/287.000; 544/311.000; 546/141.000; 546/243.000; 546/246.000; 548/477.000; 548/546.000
NCL NCLM: 544/267.000
NCLS: 544/257.000; 544/285.000; 544/286.000; 544/287.000; 544/311.000; 546/141.000; 546/243.000; 546/246.000; 548/477.000; 548/546.000

L24 ANSWER 6 OF 21 USPATFULL
AN 1998:68822 USPATFULL
TI Cysteine-pegylated proteins
IN Braxton, Scott M., San Mateo, CA, United States
PA Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)
PI US 5766897 980616
AI US 95-427100 950421 (8)
RLI Continuation-in-part of Ser. No. US 93-144758, filed on 29 Oct 1993, now abandoned which is a continuation-in-part of Ser. No. US 92-924294, filed on 3 Aug 1992, now patented, Pat. No. US 5457090 which is a continuation of Ser. No. US 90-542484, filed on 21 Jun 1990, now patented, Pat. No. US 5187089, issued on 16 Feb 1993
DT Utility
EXNAM Primary Examiner: Hendricks, Keith D.; Assistant Examiner: Hobbs, Lisa J.
LREP Fish & Richardson P.C.
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 2765
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods and compositions are provided for the production of PEGylated proteins having polyethylene glycol covalently bound to a cysteine residue present in either the naturally-occurring protein or introduced by site-specific mutation. Where the cysteine residue is introduced by mutation, the site for mutation is selected on the basis of the presence of an N-linked glycosylation site or the position of the residue which is normally solvent-accessible in the naturally-occurring protein.

The modified proteins produced by the method of the invention are referred to as cysteine-PEGylated proteins. Proteins PEGylated according to the invention have increased half-lives following administration to a subject and decreased immunogenicity and antigenicity, while retaining substantially the same level of biological activity as that of the naturally-occurring, unmodified protein. Modification of proteins according to methods of the invention thus provide improved pharmaceutical compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/172.100
INCLS: 435/188.000; 435/212.000; 435/219.000
NCL NCLM: 435/463.000
NCLS: 435/188.000; 435/212.000; 435/219.000

L24 ANSWER 7 OF 21 USPATFULL
AN 1998:64728 USPATFULL
TI Combined treatment of iron depletion and IgG antibody
IN Kemp, John D., Iowa City, IA, United States
PA University of Iowa Research Foundation, Iowa City, IA, United States (U.S. corporation)
PI US 5762932 980609
AI US 96-718293 960920 (8)
RLI Continuation of Ser. No. US 94-358389, filed on 19 Dec 1994, now abandoned which is a continuation-in-part of Ser. No. US 93-54679, filed on 29 Apr 1993, now abandoned which is a continuation-in-part of Ser. No. US 90-514706, filed on 26 Apr 1990, now abandoned
DT Utility
EXNAM Primary Examiner: Scheiner, Toni R.; Assistant Examiner: Bansal, Geetha P.
LREP Kohn & Associates
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN 13 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 782
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of inhibiting tumor growth includes the steps of depleting intracellular iron levels of tumor cells to increase expression of cellular transferrin receptors in tumor cells and then exposing the tumor cells to **monoclonal** IgG anti-transferrin receptor antibodies.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/143.100
INCLS: 424/144.100; 424/155.100; 424/156.100; 514/575.000; 514/626.000
NCL NCLM: 424/143.100
NCLS: 424/144.100; 424/155.100; 424/156.100; 514/575.000;

514/626.000

L24 ANSWER 8 OF 21 USPATFULL
AN 1998:51651 USPATFULL
TI Substituted amino alcohol compounds
IN Klein, J. Peter, Vashon, WA, United States
Underiner, Gail E., Brier, WA, United States
Kumar, Anil M., Seattle, WA, United States
PA Cell Therapeutics, Inc., Seattle, WA, United States (U.S. corporation)
PI US 5750575 980512
AI US 95-475721 950607 (8)
RLI Division of Ser. No. US 94-303842, filed on 8 Sep 1994, now patented, Pat. No. US 5641783 which is a continuation-in-part of Ser. No. US 93-152650, filed on 12 Nov 1993 And a continuation-in-part of Ser. No. US 93-164081, filed on 8 Dec 1993, now patented, Pat. No. US 5470878 which is a continuation-in-part of Ser. No. US 93-40820, filed on 31 Mar 1993, now abandoned
DT Utility
EXNAM Primary Examiner: Dees, Jose G.; Assistant Examiner: Cebulak, M.
LREP McDermott, Will & Emery; Faciszewski, Esq., Stephen
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN 115 Drawing Figure(s); 90 Drawing Page(s)
LN.CNT 3115
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are compounds having a straight or branched aliphatic hydrocarbon structure of formula I: ##STR1## In formula I, n is an integer from one to four and m is an integer from four to twenty. Independently, R.sub.1 and R.sub.2 are hydrogen, a straight or branched chain alkyl, alkenyl or alkynyl of up to twenty carbon atoms in length or --(CH.sub.2).sub.w R.sub.5. If R.sub.1 or R.sub.2 is --(CH.sub.2).sub.w R.sub.5, w may be an integer from one to twenty and R.sub.5 may be an hydroxyl, halo, C.sub.1-8 alkoxyl group or a substituted or unsubstituted carbocycle or heterocycle. Alternatively, R.sub.1 and R.sub.2 may jointly form a substituted or unsubstituted, saturated or unsaturated heterocycle having from four to eight carbon atoms, N being a hetero atom of the resulting heterocyle. R.sub.3 may be either hydrogen or C.sub.1-3. In the compounds, a total sum of carbon atoms comprising R.sub.1 or R.sub.2, (CH.sub.2).sub.n and (CH.sub.2).sub.m does not exceed forty. R.sub.4 is a carbocycle comprising a substituted or unsubstituted ring system, the ring system having a single ring or two fused rings, a ring comprising from three to seven ring atoms. The disclosed compounds are effective agents to inhibit undesirable responses to cell stimuli.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 514/617.000
INCLS: 514/653.000; 564/182.000; 564/355.000; 564/361.000
NCL NCLM: 514/617.000
NCLS: 514/653.000; 564/182.000; 564/355.000; 564/361.000

L24 ANSWER 9 OF 21 USPATFULL
AN 1998:27768 USPATFULL
TI Treatment of tumors of the central nervous system with immunotoxins
IN Johnson, Virginia, College Park, MD, United States
Youle, Richard J., Chevy Chase, MD, United States
PA The United States of America as represented by the Secretary of the Department of Health and Human Services, Washington, DC, United States (U.S. government)
PI US 5728383 980317
AI US 94-258712 940613 (8)
RLI Continuation of Ser. No. US 92-925417, filed on 10 Aug 1992, now patented, Pat. No. US 5352447 which is a continuation of Ser. No. US 89-401412, filed on 1 Sep 1989, now abandoned which is a continuation-in-part of Ser. No. US 89-301376, filed on 25 Jan 1989, now patented, Pat. No. US 5208021 which is a division of Ser. No. US 88-236225, filed on 25 Aug 1988, now abandoned which is a continuation-in-part of Ser. No. US 87-105172, filed on 5 Oct 1987, now abandoned
DT Utility
EXNAM Primary Examiner: Hutzell, Paula K.; Assistant Examiner: Bakalyar, Heather A.
LREP Klarquist, Sparkman, Campbell, Leigh & Whinston
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 11 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 1097
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Potent and specific immunotoxins are prepared by conjugation of moieties binding to receptors on the surface of tumor cells to a mutant diphtheria toxin having A-chain translocation activity, but lacking membrane-binding activity. The immunotoxins are used to treat primary tumors of neurologic origin, metastatic tumors of small cell lung carcinoma or breast carcinoma origin, leptomeningeal leukemia and leptomeningeal carcinomatosis. The preferred route of **administration** of the immunotoxin is to a compartment of the body containing cerebrospinal fluid.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/183.100
INCLS: 424/832.000; 424/194.100; 424/195.110; 514/008.000; 514/012.000; 514/021.000; 530/391.700; 530/394.000; 530/380.000; 530/388.100; 530/388.200; 530/388.220; 530/387.700; 530/388.800; 530/363.000

NCL NCLM: 424/183.100
NCLS: 424/194.100; 424/195.110; 424/832.000; 514/008.000; 514/012.000; 514/021.000; 530/363.000; 530/380.000; 530/387.700; 530/388.100; 530/388.200; 530/388.220; 530/388.800; 530/391.700; 530/394.000

L24 ANSWER 10 OF 21 USPATFULL
AN 97:54233 USPATFULL
TI Substituted amino alcohol compounds
IN Klein, J. Peter, Vashon, WA, United States
Underiner, Gail E., Brier, WA, United States
Kumar, Anil M., Seattle, WA, United States
PA Cell Therapeutics, Inc., Seattle, WA, United States (U.S. corporation)
PI US 5641783 970624
AI US 94-303842 940908 (8)
RLI Continuation-in-part of Ser. No. US 93-152650, filed on 12 Nov 1993 And Ser. No. US 93-164081, filed on 8 Dec 1993, now patented, Pat. No. US 5470878
DT Utility
EXNAM Primary Examiner: Raymond, Richard L.; Assistant Examiner: Cebulak, Mary C.
LREP Faciszewski, Stephen; Oster, Jeffrey B.
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN 115 Drawing Figure(s); 88 Drawing Page(s)
LN.CNT 3206
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are compounds having a straight or branched aliphatic hydrocarbon structure of formula I: ##STR1## In formula I, n is an integer from one to four and m is an integer from four to twenty. Independently, R.sub.1 and R.sub.2 are hydrogen, a straight or branched chain alkyl, alkenyl or alkynyl of up to twenty carbon atoms in length or --(CH.sub.2).sub.w R.sub.5. If R.sub.1 or R.sub.2 is --(CH.sub.2).sub.w R.sub.5, w may be an integer from one to twenty and R.sub.5 may be an hydroxyl, halo, C.sub.1-8 alkoxyl group or a substituted or unsubstituted carbocycle or heterocycle. Alternatively, R.sub.1 and R.sub.2 may jointly form a substituted or unsubstituted, saturated or unsaturated heterocycle having from four to eight carbon atoms, N being a hetero atom of the resulting heterocycle. R.sub.3 may be either hydrogen or C.sub.1-3. In the compounds, a total sum of carbon atoms comprising R.sub.1 or R.sub.2, (CH.sub.2).sub.n and (CH.sub.2).sub.m does not exceed forty. R.sub.4 is a terminal moiety comprising a substituted or unsubstituted, oxidized or reduced ring system, the ring system having a single ring or two to three fused rings, a ring comprising from three to seven ring atoms. The disclosed compounds are effective agents to inhibit undesirable responses to cell stimuli.

Searcher : Shears 308-4994

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 514/263.000

INCLS: 514/183.000; 514/222.500; 514/223.500; 514/224.200;
514/226.800; 514/227.500; 514/228.800; 514/229.200;
514/230.500; 514/230.800; 514/237.800; 514/241.000;
514/242.000; 514/243.000; 514/246.000; 514/247.000;
514/248.000; 514/249.000; 514/255.000; 514/256.000;
514/258.000; 514/259.000; 514/261.000; 514/262.000;
514/263.000; 514/270.000; 514/274.000; 514/297.000;
514/300.000; 514/301.000; 514/302.000; 514/303.000;
514/306.000; 514/307.000; 514/311.000; 514/312.000;
514/315.000; 514/345.000; 514/351.000; 514/357.000;
514/359.000; 514/360.000; 514/361.000; 514/362.000;
514/363.000; 514/364.000; 514/365.000; 514/367.000;
514/369.000; 514/372.000; 514/373.000; 514/374.000;
514/375.000; 514/376.000; 514/378.000; 514/379.000;
514/380.000; 514/381.000; 514/383.000; 514/389.000;
514/394.000; 514/395.000; 514/398.000; 514/399.000;
514/401.000; 514/404.000; 514/406.000; 514/413.000;
514/415.000; 514/416.000; 514/418.000; 514/423.000;
514/424.000; 514/425.000; 514/427.000; 514/428.000;
544/001.000; 544/002.000; 544/003.000; 544/008.000;
544/053.000; 544/063.000; 544/065.000; 544/066.000;
544/067.000; 544/090.000; 544/091.000; 544/162.000;
544/215.000; 544/216.000; 544/219.000; 544/220.000;
544/224.000; 544/235.000; 544/239.000; 544/254.000;
544/255.000; 544/257.000; 544/262.000; 544/272.000;
544/277.000; 544/278.000; 544/280.000; 544/283.000;
544/286.000; 544/301.000; 544/311.000; 544/335.000;
544/336.000; 544/350.000; 544/353.000; 544/385.000;
544/401.000; 546/102.000; 546/113.000; 546/114.000;
546/115.000; 546/117.000; 546/118.000; 546/119.000;
546/122.000; 546/138.000; 546/139.000; 546/150.000;
546/153.000; 546/157.000; 546/164.000; 546/176.000;
546/178.000; 546/242.000; 546/243.000; 546/246.000;
546/264.000; 546/300.000; 546/334.000; 548/100.000;
548/123.000; 548/125.000; 548/127.000; 548/128.000;
548/131.000; 548/134.000; 548/146.000; 548/153.000;
548/179.000; 548/186.000; 548/207.000; 548/214.000;
548/215.000; 548/217.000; 548/221.000; 548/225.000;
548/228.000; 548/229.000; 548/235.000; 548/237.000;
548/240.000; 548/241.000; 548/243.000; 548/247.000;
548/252.000; 548/267.200; 548/267.800; 548/303.700;
548/306.400; 548/307.100; 548/309.700; 548/319.100;
548/323.500; 548/340.100; 548/348.100; 548/349.100;
548/356.100; 548/370.100; 548/375.100; 548/379.400;
548/452.000; 548/453.000; 548/470.000; 548/482.000;
548/485.000; 548/486.000; 548/491.000; 548/503.000;

Searcher : Shears 308-4994

548/532.000; 548/543.000; 548/546.000; 548/550.000;
548/565.000; 548/566.000

NCL NCLM: 514/263.000

NCLS: 514/183.000; 514/222.500; 514/223.500; 514/224.200;
514/226.800; 514/227.500; 514/228.800; 514/229.200;
514/230.500; 514/230.800; 514/237.800; 514/241.000;
514/242.000; 514/243.000; 514/246.000; 514/247.000;
514/248.000; 514/249.000; 514/255.000; 514/256.000;
514/258.000; 514/259.000; 514/261.000; 514/262.000;
514/270.000; 514/274.000; 514/297.000; 514/300.000;
514/301.000; 514/302.000; 514/303.000; 514/306.000;
514/307.000; 514/311.000; 514/312.000; 514/315.000;
514/345.000; 514/351.000; 514/357.000; 514/359.000;
514/360.000; 514/361.000; 514/362.000; 514/363.000;
514/364.000; 514/365.000; 514/367.000; 514/369.000;
514/372.000; 514/373.000; 514/374.000; 514/375.000;
514/376.000; 514/378.000; 514/379.000; 514/380.000;
514/381.000; 514/383.000; 514/389.000; 514/394.000;
514/395.000; 514/398.000; 514/399.000; 514/401.000;
514/404.000; 514/406.000; 514/413.000; 514/415.000;
514/416.000; 514/418.000; 514/423.000; 514/424.000;
514/425.000; 514/427.000; 514/428.000; 544/001.000;
544/002.000; 544/003.000; 544/008.000; 544/053.000;
544/063.000; 544/065.000; 544/066.000; 544/067.000;
544/090.000; 544/091.000; 544/162.000; 544/215.000;
544/216.000; 544/219.000; 544/220.000; 544/224.000;
544/235.000; 544/239.000; 544/254.000; 544/255.000;
544/257.000; 544/262.000; 544/272.000; 544/277.000;
544/278.000; 544/280.000; 544/283.000; 544/286.000;
544/301.000; 544/311.000; 544/335.000; 544/336.000;
544/350.000; 544/353.000; 544/385.000; 544/401.000;
546/102.000; 546/113.000; 546/114.000; 546/115.000;
546/117.000; 546/118.000; 546/119.000; 546/122.000;
546/138.000; 546/139.000; 546/150.000; 546/153.000;
546/157.000; 546/164.000; 546/176.000; 546/178.000;
546/242.000; 546/243.000; 546/246.000; 546/264.000;
546/300.000; 546/334.000; 548/100.000; 548/123.000;
548/125.000; 548/127.000; 548/128.000; 548/131.000;
548/134.000; 548/146.000; 548/153.000; 548/179.000;
548/186.000; 548/207.000; 548/214.000; 548/215.000;
548/217.000; 548/221.000; 548/225.000; 548/228.000;
548/229.000; 548/235.000; 548/237.000; 548/240.000;
548/241.000; 548/243.000; 548/247.000; 548/252.000;
548/267.200; 548/267.800; 548/303.700; 548/306.400;
548/307.100; 548/309.700; 548/319.100; 548/323.500;
548/340.100; 548/348.100; 548/349.100; 548/356.100;
548/370.100; 548/375.100; 548/379.400; 548/452.000;
548/453.000; 548/470.000; 548/482.000; 548/485.000;
548/486.000; 548/491.000; 548/503.000; 548/532.000;

548/543.000; 548/546.000; 548/550.000; 548/565.000;
548/566.000

L24 ANSWER 11 OF 21 USPATFULL
AN 96:111463 USPATFULL
TI Enatiomerically pure hydroxylated xanthine compounds
IN Bianco, James A., Seattle, WA, United States
Woodson, Paul, Bothell, WA, United States
Porubek, David, Edmonds, WA, United States
Singer, Jack, Seattle, WA, United States
PA Cell Therapeutics, Inc., Seattle, WA, United States (U.S. corporation)
PI US 5580874 961203
AI US 95-457685 950601 (8)
RLI Division of Ser. No. US 94-343810, filed on 22 Nov 1994, now abandoned which is a division of Ser. No. US 94-307554, filed on 16 Sep 1994 which is a continuation of Ser. No. US 93-13977, filed on 4 Feb 1993, now abandoned which is a continuation-in-part of Ser. No. US 92-926665, filed on 7 Aug 1992, now abandoned which is a continuation-in-part of Ser. No. US 92-846354, filed on 4 Mar 1992, now abandoned
DT Utility
EXNAM Primary Examiner: Criares, Theodore J.
LREP Faciszewski, Stephen
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 22 Drawing Figure(s); 22 Drawing Page(s)
LN.CNT 1733
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Them is disclosed compounds and pharmaceutical compositions that is R enantiomer of an .omega.-1 alcohol of a straight chain alkyl (C.sub.5-8) substituted at the 1-position of 3,7-disubstituted xanthine. The inventive compounds are effective in treating the side effects of immunosuppressive agent and interleukin-2 therapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/263.000
NCL NCLM: 514/263.000

L24 ANSWER 12 OF 21 USPATFULL
AN 96:109072 USPATFULL
TI Methods and compositions concerning homogenous immunotoxin preparations
IN Ghetie, Victor F., Dallas, TX, United States
Uhr, Jonathan W., Dallas, TX, United States
Vitetta, Ellen S., Dallas, TX, United States
PA Board of Regents, The University of Texas, Austin, TX, United States (U.S. corporation)
PI US 5578706 961126

AI US 93-147768 931104 (8)
DT Utility
EXNAM Primary Examiner: Scheiner, Toni R.
LREP Arnold White & Durkee
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 1272
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Immunotoxin preparations are described in which the preparations are enriched for a single species of immunotoxin. Also described are methods for the preparation of the substantially purified immunotoxins (ITs). Also disclosed are methods for determining the most effective species of immunotoxin conjugates for treated diseases and pharmaceutical preparations for such treatments.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 530/391.700
INCLS: 530/391.100; 424/178.100; 424/183.100
NCL NCLM: 530/391.700
NCLS: 424/178.100; 424/183.100; 530/391.100

L24 ANSWER 13 OF 21 USPATFULL
AN 95:94924 USPATFULL
TI Methods of inhibiting transplant rejection in mammals using rapamycin and derivatives and prodrugs thereof
IN Calne, Roy, 22 Barrow Road, Cambridge, England CB2 2AS
PI US 5461058 951024
AI US 95-377163 950124 (8)
RLI Division of Ser. No. US 94-192648, filed on 7 Feb 1994, now patented, Pat. No. US 5403833, issued on 4 Apr 1995 which is a division of Ser. No. US 93-9570, filed on 26 Jan 1993, now patented, Pat. No. US 5308847 which is a division of Ser. No. US 91-738960, filed on 31 Jul 1991, now patented, Pat. No. US 5212155, issued on 18 May 1993 which is a division of Ser. No. US 89-362354, filed on 6 Jun 1989, now patented, Pat. No. US 5100899, issued on 31 Mar 1992
DT Utility
EXNAM Primary Examiner: Goldberg, Jerome D.
LREP Darby & Darby
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 425
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a method of inhibiting organ or tissue transplant rejection in a mammal in need thereof, comprising **adminis ring** to said mammal a transplant rejection inhibiting amount of rapamycin. Also disclosed is a method of

inhibiting organ or tissue transplant rejection in a mammal in need thereof, comprising **administering** to said mammal (a) an amount of rapamycin in combination with (b) an amount of one or more other chemotherapeutic agents for inhibiting transplant rejection, e.g., azathioprine, corticosteroids, cyclosporin and FK506, said amounts of (a) and (b) together being effective to inhibit transplant rejection and to maintain inhibition of transplant rejection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/291.000
NCL NCLM: 514/291.000

L24 ANSWER 14 OF 21 USPATFULL
AN 95:29635 USPATFULL
TI Methods of inhibiting transplant rejecton in mammals using rapamycin and derivatives and prodrugs thereof
IN Calne, Sir Roy, 22 Arrow Rd., Cambridge, England CB2 2AS
PI US 5403833 950404
AI US 94-192648 940207 (8)
RLI Division of Ser. No. US 93-9570, filed on 26 Jan 1993, now patented, Pat. No. US 5308847 which is a division of Ser. No. US 91-738960, filed on 31 Jul 1991, now patented, Pat. No. US 5212155, issued on 18 May 1993 which is a division of Ser. No. US 89-362354, filed on 6 Jun 1989, now patented, Pat. No. US 5100899, issued on 31 Mar 1992
DT Utility
EXNAM Primary Examiner: Goldberg, Jerome D.
LREP Darby & Darby
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 412
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a method of inhibiting organ or tissue transplant rejection in a mammal in need thereof, comprising **administering** to said mammal a transplant rejection inhibiting amount of rapamycin. Also disclosed is a method of inhibiting organ or tissue transplant rejection in a mammal in need thereof, comprising **administering** to said mammal (a) an amount of rapamycin in combination with (b) an amount of one or more other chemotherapeutic agents for inhibiting transplant rejection, e.g., azathioprine, corticosteroids, cyclosporin and FK506, said amounts of (a) and (b) together being effective to inhibit transplant rejection and to maintain inhibition of transplant rejection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/171.000

INCLS: 514/291.000
NCL NCLM: 514/171.000
NCLS: 514/291.000

L24 ANSWER 15 OF 21 USPATFULL
AN 94:86179 USPATFULL
TI Immunotoxins for treatment of intracranial lesions and as adjunct to chemotherapy
IN Johnson, Virginia, College Park, MD, United States
Youle, Richard J., Garrett Park, MD, United States
PA The United States of America as represented by the Secretary of the Department of Health and Human Services, Washington, DC, United States (U.S. government)
PI US 5352447 941004
AI US 92-92541 920810 (7)
RLI Continuation of Ser. No. US 89-401412, filed on 1 Sep 1989, now abandoned which is a continuation-in-part of Ser. No. US 89-301376, filed on 25 Jan 1989, now patented, Pat. No. US 5208021 which is a division of Ser. No. US 88-236225, filed on 25 Aug 1988, now abandoned which is a continuation-in-part of Ser. No. US 87-105172, filed on 5 Oct 1987, now abandoned
DT Utility
EXNAM Primary Examiner: Kim, Kay K.
LREP Birch, Stewart, Kolasch & Birch
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 11 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 1102
AB A potent and specific immunotoxin is prepared by coupling a binding-site inactivated diphtheria toxin (CRM 107) to a new binding moiety consisting of transferrin or a **monoclonal** antibody against the human transferrin receptor. These immunotoxins are tumor specific and lack the nonspecific toxicity produced by the binding activity of the native toxin. The immunotoxin is useful in treating primary brain tumors, metastatic tumors to the brain, CSF-borne tumors, leptomeningeal leukemia and leptomeningeal carcinomatosis.

INCL INCLM: 424/183.100
INCLS: 514/008.000; 514/012.000; 514/021.000; 530/391.700; 530/394.000; 424/832.000
NCL NCLM: 424/183.100
NCLS: 424/832.000; 514/008.000; 514/012.000; 514/021.000; 530/391.700; 530/394.000

L24 ANSWER 16 OF 21 USPATFULL
AN 94:37944 USPATFULL
TI Methods of inhibiting transplant rejection in mammals using rapamycin and derivatives and prodrugs thereof

IN Calne, Sir Roy, 22 Arrow Rd., Cambridge, England CB2 2AS
PI US 5308847 940503
AI US 93-9570 930126 (8)
RLI Division of Ser. No. US 91-738960, filed on 31 Jul 1991, now patented, Pat. No. US 5212155 which is a division of Ser. No. US 89-362354, filed on 6 Jun 1989, now patented, Pat. No. US 5100899
DT Utility
EXNAM Primary Examiner: Goldberg, Jerome D.
LREP Darby & Darby
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 398
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a method of inhibiting organ or tissue transplant rejection in a mammal in need thereof, comprising **administering** to said mammal a transplant rejection inhibiting amount of rapamycin. Also disclosed is a method of inhibiting organ or tissue transplant rejection in a mammal in need thereof, comprising **administering** to said mammal (a) an amount of rapamycin in combination with (b) an amount of one or more other chemotherapeutic agents for inhibiting transplant rejection, e.g., azathioprine, corticosteroids, cyclosporin and FK506, said amounts of (a) and (b) together being effective to inhibit transplant rejection and to maintain inhibition of transplant rejection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/262.000
INCLS: 514/291.000
NCL NCLM: 514/262.000
NCLS: 514/291.000

L24 ANSWER 17 OF 21 USPATFULL
AN 93:39979 USPATFULL
TI Methods of inhibiting transplant rejection in mammals using rapamycin and derivatives and prodrugs thereof
IN Calne, Roy, Cambridge, England CB2 2AS
PI US 5212155 930518
AI US 91-738960 910731 (7)
RLI Division of Ser. No. US 89-362354, filed on 6 Jun 1989, now patented, Pat. No. US 5100899
DT Utility
EXNAM Primary Examiner: Goldberg, Jerome D.
LREP Darby & Darby
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 396

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a method of inhibiting organ or tissue transplant rejection in a mammal in need thereof, comprising **administering** to said mammal a transplant rejection inhibiting amount of rapamycin. Also disclosed is a method of inhibiting organ or tissue transplant rejection in a mammal in need thereof, comprising **administering** to said mammal (a) an amount of rapamycin in combination with (b) an amount of one or more other chemotherapeutic agents for inhibiting transplant rejection, e.g., azathioprine, corticosteroids, cyclosporin and FK506, said amounts of (a) and (b) together being effective to inhibit transplant rejection and to maintain inhibition of transplant rejection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/011.000
INCLS: 514/291.000
NCL NCLM: 514/011.000
NCLS: 514/291.000

L24 ANSWER 18 OF 21 USPATFULL
AN 93:35474 USPATFULL
TI Method of preparing diphtheria immunotoxins
IN Johnson, Virginia G., College Park, MD, United States
Greenfield, Larry, Emeryville, CA, United States
Youle, Richard J., Garrett Park, MD, United States
Laird, Walter, Pinole, CA, United States
PA The United States of America as represented by the Secretary of the Department of Health and Human Services, Washington, DC, United States (U.S. government)
Cetus Corporation, Emeryville, CA, United States (U.S. corporation)
PI US 5208021 930504
AI US 89-301376 890125 (7)
RLI Division of Ser. No. US 88-236225, filed on 25 Aug 1988, now abandoned which is a continuation-in-part of Ser. No. US 87-105172, filed on 5 Oct 1987, now abandoned
DT Utility
EXNAM Primary Examiner: Brown, Johnnie R.; Assistant Examiner: Mohamed, Abdel A.
LREP Birch, Stewart, Kolasch & Birch
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 14 Drawing Figure(s); 9 Drawing Page(s)
LN.CNT 1266
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A potent and specific immunotoxin is prepared by coupling an inactivated diphteria toxin to a binding moiety such as a **monoclonal** antibody or transferrin. The immunotoxins are

specific for human tumors and leukemias and are indistinguishable in cell toxicity from that of the native toxin linked to the binding domain without the toxicity to other cells. The immunotoxin is useful in treating graft versus host disease as well as selectively killing tumor cells, such as medulloblastoma and glioblastoma cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/085.910
INCLS: 424/085.500; 424/085.800; 530/388.100; 530/388.220; 530/390.100; 530/409.000; 530/412.000; 530/417.000; 530/820.000; 435/069.100; 436/548.000
NCL NCLM: 530/391.900
NCLS: 424/085.500; 424/179.100; 435/069.100; 436/548.000; 530/300.000; 530/388.100; 530/388.220; 530/390.100; 530/394.000; 530/409.000; 530/412.000; 530/417.000; 530/820.000

L24 ANSWER 19 OF 21 USPATFULL
AN 92:92536 USPATFULL
TI Methods and compositions for the treatment of Hodgkin's disease
IN Thorpe, Philip, Ruislip, United Kingdom
Engert, Andreas, London, United Kingdom
PA Imperial Cancer Research Technology, London, United Kingdom (non-U.S. corporation)
PI US 5165923 921124
AI US 89-440050 891120 (7)
DT Utility
EXNAM Primary Examiner: Nucker, Christine; Assistant Examiner: Kim, Kay K.
LREP Arnold, White & Durkee
CLMN Number of Claims: 29
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 2191
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are methods and compositions for the treatment of Hodgkin's disease and processes involving Hodgkin's disease cells or Reed-Sternberg cells, through specific elimination of Hodgkin's disease cells through the application of immunotoxin technology. The compositions of the invention include toxin conjugates composed of a Hodgkin's disease cell binding ligand conjugated to a toxin A chain moiety such as ricin A chain or deglycosylated ricin A chain, by means of a cross-linker or other conjugation which includes a disulfide bond. In preferred aspects of the invention, therapeutic amounts of conjugates composed of a CD-30 or IRac antibody or fragment thereof conjugated to deglycosylated A chain by means of an SMPT linker is **administered** to a Hodgkin's disease patient so as to specifically eliminate

Hodgkin's disease cells without exerting significant toxicity against non-tumor cells. Also disclosed are particular **hybridomas** and **monoclonal** antibodies, and associated methodology, which may be employed, e.g., in the preparation of these immunotoxins as well as other uses such as diagnostic applications.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/085.910
INCLS: 530/391.900; 530/388.700; 530/388.730; 530/388.750
NCL NCLM: 424/179.100
NCLS: 424/153.100; 424/154.100; 424/178.100; 530/388.700; 530/388.730; 530/388.750; 530/391.900

L24 ANSWER 20 OF 21 USPATFULL
AN 92:25361 USPATFULL
TI Methods of inhibiting transplant rejection in mammals using rapamycin and derivatives and prodrugs thereof
IN Calne, Roy, 22 Arrow Road, Cambridge, England CB22AS
PI US 5100899 920331
AI US 89-362354 890606 (7)
DT Utility
EXNAM Primary Examiner: Goldberg, Jerome D.
LREP Darby & Darby
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 389
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a method of inhibiting organ or tissue transplant rejection in a mammal in need thereof, comprising **administering** to said mammal a transplant rejection inhibiting amount of rapamycin. Also disclosed is a method of inhibiting organ or tissue transplant rejection in a mammal in need thereof, comprising **administering** to said mammal (a) an amount of rapamycin in combination with (b) an amount of one or more other chemotherapeutic agents for inhibiting transplant rejection, e.g., azathioprine, corticosteroids, cyclosporin and FK506, said amounts of (a) and (b) together being effective to inhibit transplant rejection and to maintain inhibition of transplant rejection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/291.000
NCL NCLM: 514/291.000

L24 ANSWER 21 OF 21 USPATFULL
AN 87:71534 USPATFULL
TI Products and methods for treatment of cancer

IN Terman, David S., 25371 Outlook Dr., Carmel, CA, United States 93923
Balint, Joseph P., 169 Crooks Ave., Clifton, NJ, United States 07011
Langone, John J., 7735 Candlegreen, Houston, TX, United States 77071

PI US 4699783 871013
AI US 83-542239 831014 (6)
RLI Continuation-in-part of Ser. No. US 83-472362, filed on 11 Mar 1983, now abandoned which is a continuation-in-part of Ser. No. US 82-366436, filed on 7 Apr 1982, now abandoned
DT Utility
EXNAM Primary Examiner: Hazel, Blondel
LREP Fulbright & Jaworski
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 2130
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are compositions for the treatment of cancer, such as lymphomas and solid tumors, methods of producing these compositions, and methods and regimens in using these compositions in the treatment of hosts having cancer. The compositions are (1) tumor immune preparations which can be prepared by acidification or alkalinization of an enriched immunoglobulin effluent from forced flow electrophoresis of plasma from a normal or a tumor bearing host, (2) tumor immune globulin which can be prepared by acidifying a Cohn gamma globulin fraction from a normal or a tumor bearing host, (3) protein A-IgG preparations which can be prepared by perfusion of plasma over protein A from staphylococcus aureus Cowans I and precipitating the complex or by incubating protein A and purified IgG or IgG in plasma, (4) tumor immune plasma preparations which may be prepared by acidification of plasma from normal or tumor bearing hosts, and (5) zymosan activated plasma which can be prepared by incubating plasma with zymosan and then removing the zymosan. Infusing of the compositions alone or in combination with each other and with various chemotherapeutic agents has resulted in tumoricidal reactions, objective anti-tumor effects, and sustained tumor regressions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/085.000
INCLS: 424/101.000; 530/387.000
NCL NCLM: 424/178.100
NCLS: 530/389.700; 530/413.000; 530/419.000; 530/421.000

=> d his l25-

(FILE 'BIOSIS, MEDLINE, EMBASE, LIFESCI, BIOTECHDS, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, PROMT, TOXLIT, TOXLINE, DRUGU, DRUGNL, DRUGLAUNCH, DRUGB, CANCERLIT' ENTERED AT 16:41:41 ON 07 DEC 1998)

L25 3046 SEA ABB=ON PLU=ON L13
L26 760 SEA ABB=ON PLU=ON L25 AND (BR96 OR (BR OR CHIBR OR HBR)(W) 96 OR CHIBR96 OR HBR96 OR HB10460 OR HB10036 OR HB(W)(10460 OR 10036) OR MOAB OR MAB OR MONOCLON? OR HYBRIDOMA)
L27 7 SEA ABB=ON PLU=ON L26 AND (LE OR LEY OR LEX)
L28 204 SEA ABB=ON PLU=ON L26 AND ADMIN?
L29 50 SEA ABB=ON PLU=ON L28 AND (IMMUNOTHERAP? OR IMMUN? THERAP?)
L30 57 SEA ABB=ON PLU=ON L27 OR L29
L31 28 DUP REM L30 (29 DUPLICATES REMOVED)

L31 ANSWER 1 OF 28 BIOTECHDS COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 98-05259 BIOTECHDS
TI **Inhibiting immunoglobulin**-induced **toxicity** resulting from **immunotherapy**; using humanized antibody or chimeric antibody produced by antibody engineering
AU Rosok M J; Yelton D E
PA Bristol-Squibb
LO New York, NY, USA.
PI WO 9805787 12 Feb 1998
AI WO 97-US13562 1 Aug 1997
PRAI US 96-23033 2 Aug 1996
DT Patent
LA English
OS WPI: 98-145622 [13]
AN 98-05259 BIOTECHDS
AB A new method for **inhibiting immunoglobulin**-induced **toxicity** resulting from **Ig immunotherapy** involves: **administering** to a subject an **Ig** molecule having a variable and a constant regions, where the **Ig** is modified prior to **administration** by structurally altering multiple **toxicity** associated domains in the constant region so that **Ig**-induced **toxicity** is **inhibited**; preventing **Ig**-induced **toxicity** resulting from **Ig immunotherapy** in a subject, by selecting an **Ig** or **Ig** fusion protein which recognizes and binds to a target which is associated with the disease, structurally altering multiple **toxicity** associated domains in the CH2 domain of the constant region of the **Ig**, and **administering** the structurally altered **Ig** or **Ig** fusion protein under conditions so that the structurally altered **Ig** fusion protein recognizes and binds the target, alleviating symptoms associated with the disease,

where the structural alteration of the CH2 domain of the constant region prevents **Ig**-induced **toxicity** in a subject; and **BR96** antibodies (humanized or chimeric). Nucleic acid encoding the antibody, a plasmid, a host/vector system and a pharmaceutical composition are also claimed. (135pp)

L31 ANSWER 2 OF 28 MEDLINE DUPLICATE 2
AN 1998268584 MEDLINE
DN 98268584
TI Antibody responses in melanoma patients immunized with an anti-idiotype antibody mimicking disialoganglioside GD2.
AU Foon K A; Sen G; Hutchins L; Kashala O L; Baral R; Banerjee M; Chakraborty M; Garrison J; Reisfeld R A; Bhattacharya-Chatterjee M
CS Department of Internal Medicine, Lucille Parker Markey Cancer Center, University of Kentucky Medical Center, Lexington 40536-0093, USA.
NC R01CA-72018-02 (NCI)
SO Clin Cancer Res, (1998 May) 4 (5) 1117-24.
Journal code: C2H. ISSN: 1078-0432.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199809
EW 19980903
AB We initiated a clinical trial for patients with advanced malignant melanoma treated with an anti-idiotype antibody that mimics the disialoganglioside GD2. We report the clinical and immune responses of the first 12 patients entered into this trial. Patients received 1-, 2-, 4-, or 8-mg doses of the anti-idiotype antibody mixed with 100 microg of QS-21 adjuvant every other week, four times, and then monthly. Twelve patients have been on trial for 2-23 months, and all of them have generated immune responses. Patients were removed from the study if they demonstrated disease progression. Hyperimmune sera from all 12 patients revealed an anti-anti-idiotypic Ab3 response, as demonstrated by the **inhibition** of Ab2 binding to Ab1 by patients' immune sera. To further test the anti-anti-idiotypic response, patients' Ab3 antibodies were affinity purified on Sepharose 4B columns containing adsorbed immunizing anti-idiotype **immunoglobulin**. Purified Ab3 of all patients studied **inhibited** binding of Ab1 to a GD2-positive cell line. Purified Ab3 also **inhibited** binding of Ab1 to purified GD2, in a manner comparable to equal quantities of purified Ab1. The patient Ab3 was truly an Ab1' because it specifically bound to purified disialoganglioside GD2. The isotypic specificity of the Ab3 antibody was predominantly **IgG**, with only minimal **IgM**. The predominant **IgG** subclass was IgG1, with approximately equal quantities of IgG2, IgG3, and IgG4. These Ab3

antibodies reacted specifically with tumor cells expressing GD2 by immune flow cytometry and immunoperoxidase assays. Five patients' Ab3 antibodies studied for antibody-dependent cellular cytotoxicity were positive. One patient had a complete clinical response, with resolution of soft tissue disease, and six patients had stable disease, ranging from 9 to 23 months, and are being continued on vaccine therapy. **Toxicity** consisted of local reaction at the site of the injection, including induration and pain that generally resolved within a few days. Mild fever and chills were observed in 75% of the patients but rarely required acetaminophen. There was no additional **toxicity**, including abdominal pain that was previously seen with infusion of murine **monoclonal** anti-GD2 antibody. Current trials include patients with stage III melanoma and small cell lung cancer. Future trials will attempt to enhance the antitumor response by the addition of interleukin 2, granulocyte macrophage colony-stimulating factor, and other cytokines, together with the 1A7 vaccine.

L31 ANSWER 3 OF 28 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.
AN 1998004762 EMBASE
TI Therapy for colon carcinoma xenografts with bispecific antibody-targeted, iodine-131-labeled bivalent hapten.
AU Gautherot E.; Bouhou J.; Le Doussal J.-M.; Manetti C.; Martin M.; Rouvier E.; Barbet J.
CS E. Gautherot, Imaging and Therapeutics Department, IMMUNOTECH SA, 130 Avenue de Lattre de Tassigny, 13276 Marseille Cedex 9, France
SO Cancer, (1997) 80/12 SUPPL. (2618-2623).
Refs: 18
ISSN: 0008-543X CODEN: CANCAR
CY United States
DT Journal; Conference Article
FS 016 Cancer
023 Nuclear Medicine
026 Immunology, Serology and Transplantation
037 Drug Literature Index
048 Gastroenterology
LA English
SL English
AB BACKGROUND. One of the main limitations of radioimmunotherapy (RIT) is the secondary **toxicity** related to the poor therapeutic indices achieved with labeled whole **immunoglobulin** (**Ig**)G or F(ab')2 fragments. To overcome this problem, we have developed a two-step targeting method, which we refer to as the Affinity Enhancement System (AES), using a radiolabeled bivalent hapten and a bispecific antibody recognizing the hapten and a target cell antigen. This method has been applied successfully to immunoscintigraphy in carcinoembryonic antigen (CEA)-expressing carcinoma patients and increased tumor to normal tissue uptake ratios have been achieved. The aim of the current study was to

evaluate the application of AES to RIT of CEA- expressing solid tumors in an animal model. METHODS. Nude mice grafted with LS174T human colorectal carcinoma were treated either with 111 megabecquerels (MBq) of iodine-131 labeled bivalent diethylenetriamine pentaacetic acid (DTPA) hapten 20 hours after pretargeting by antiCEA x anti-DTPA-indium bispecific antibody or 12 MBq of iodine-131 labeled anti- CEA **IgG**. RESULTS. Treatment with the **IgG** induced only a growth delay of 53 .+-. 5 days but all tumors progressed. Treatment with the AES was highly efficient because tumor growth **inhibition** was achieved over 150 days. Hematologic and overall **toxicity** of both treatments were equivalent. CONCLUSIONS. The long term tumor regression consecutive to AES RIT represents a very significant improvement over the use of directly labeled **IgG**. **Toxicity** consecutive to AES or **IgG** RIT were similar despite an **administered** activity nearly ten times higher with the AES. However, given the efficacy of the AES treatment, a lower dose may afford lower **toxicity** and significant antitumor effect.

L31 ANSWER 4 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS
AN 98:80489 BIOSIS
DN 01080489
TI Clinical experience with CD64-directed **immunotherapy**. An overview.
AU Curnow R T
CS Medarex Inc., Annadale, NJ 08801, USA
SO Cancer Immunology Immunotherapy 45 (3-4). 1997. 210-215. ISSN: 0340-7004
LA English
AB The class I **IgG** receptor (Fc-gamma-RI or CD64 receptor), which is present on key cytotoxic effector cells, has been shown to initiate the destruction of tumor cells in vitro and has been hypothesized to play a role in the destruction of antibody-coated cells such as platelets in idiopathic thrombocytopenia purpura (ITP). This overview summarizes the clinical experience with CD64-directed **immunotherapy** in cancer patients with the bispecific antibodies MDX-447 (humanized Fab anti-CD64 times humanized Fab anti-(epidermal growth factor receptor, EGFR)) and MDX-H210 (humanized Fab anti-DC64 times Fab anti-HER2/neu), and with the anti-CD64 **monoclonal** antibody (**mAB**) MDX-33 (H22) in the modulation of monocyte CD64 in vivo. In an ongoing phase I/II open-label trial with progressive dose escalation (1-15 mg/m-2), patients with treatment refractory EGFR-positive cancers (renal cell carcinoma (RCC), head and neck, bladder, ovarian, prostate cancer and skin cancer) are treated weekly with intravenous MDX-447, with and without granulocyte-colony-stimulating factor (G-CSF). MDX-447 has been found to be immunologically active at all doses, binding to circulating monocytes and neutrophils (when given with G-CSF),

causing monocytopenia and stimulating increases in circulating plasma cytokines. MDX-447 is well tolerated, the primary **toxicities** being fever, chills, blood pressure lability, and pain/myalgias. Of 36 patients evaluable for response, 9 have experienced stable disease of 3-6 month's duration. The optimal dose and the maximal tolerated dose (MTD) have yet to be defined; dose escalation continues to define better the dose, **toxicity**, and the potential therapeutic role of this bispecific antibody. Three MDX-H210 phase II trials are currently in progress, all using the intravenous dose of 15 mg/m-2 given with granulocyte/macrophage (GM-CSF). These consist of one trial each in the treatment of RCC patients, patients with prostrate cancer, and colorectal cancer patients, all of whom have failed standard therapy. At the time of writing, 11 patients have been treated in these phase II trials. Four patients have demonstrated antitumor effects. Patients demonstrating responses include 2 with RCC and 2 with prostate cancer. One RCC patient has had a 54% reduction in size of a hepatic metastatic lesion and the other has had a 49% decrease in the size of a lung metastasis with simultaneous clearing of other non-measurable lung lesions. Regarding the two patients with prostate cancer, one has had a 90% reduction in serum prostate-specific antigen (PSA; 118-11 ng/ml), which has persisted for several months; the other patient with prostate has had a 70% reduction of serum PSA (872 ng/ml to 208 ng/ml) within the first month of treatment. Both patients have also demonstrated symptomatic improvement. In a completed phase I and in ongoing phase I/II clinical trials, patients with treatment-refractory HER2/neu positive cancers (breast, ovarian, colorectal, prostate) have been treated with MDX-H210, which has been given alone and in conjunction with G-CSF, GM-CSF, and interferon gamma (IFN-gamma). These trials have been open-label, progressive dose-escalation (0.35-135 mg/m-2) studies in which single, and more often, multiple weekly doses have been **administered**. MDX-H210 has been well tolerated, with untoward effects being primarily mild-to-moderate flu-like symptoms. The MTD has not yet been defined. MDX-H210 is immunologically active, binding to circulating monocytes, causing monocytopenia, as well as stimulating increases in plasma cytokine levels. Furthermore, some patients have evidence of active antitumor immunity following treatment with MDX-210. Antitumor effects have been seen in response to MDX-H210 **administration**; these include 1 partial, 2 minor, and 1 mixed tumor response; 15 protocol-defined stable disease responses have occurred. In a completed phase I trial, MDX-33 was **administered** as a single intravenous dose to 17 normal subjects in order to assess its potential as an immunomodulator for the treatment of idiopathic thrombocytopenia purpura and other immune disorders. Doses of 1.5, 3.0, 5.0, and 7.5 mg/m-2 were **administered**. The variables evaluated in response to MDX-33 were circulating monocyte and neutrophil coutns, monocyte CD64-mediated phagocytosis, monocyte CD64 modulation, MDX-33 pharmacokinetics, and various safety parameters. MDX-33 is well

tolerated at doses of 5.0 mg/m-2 or less, the primary **toxicities** being chills, low-grade fever, headache, and muscle aches. Persistent binding of MDX-33 to 80-99% of circulating monocytes is seen for at least 6 days; down-modulation of monocyte CD64 occurs and also lasts more than 6 days. Monocyte CD64-mediated phagocytosis is significantly **inhibited** at all doses of MDX-33. At the 3.0 mg/m-2 and 5.0 mg/m-2 dose, phagocytosis is fully **inhibited** for at least 6 days, returning to baseline levels by 20 days after dosing. These results clearly demonstrate that immunomodulation of monocyte CD64 by the **mAB** MDX-33 can be accomplished with minimal clinical **toxicity**, and further indicate the potential of MDX-33 in the treatment of ITP and other auto-immune disorders. In conclusion, the results from completed and ongoing clinical trials with the CD64-directed bsAB MDX-447 and MDX-H210 demonstrate excellent tolerability in association with promising antitumor effects in tumors that have become refractory to all available therapies. Also promising are the results from the trial of the CD64-directed **mAB**, MDX-33, which show the ability to modulate monocyte CD64 in the clinical setting. Studies are currently being conducted to elucidate the full potential of these and other approaches using CD64-directed **immunotherapy**

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L31 ANSWER 5 OF 28 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.
AN 97158034 EMBASE
TI Recent clinical trials in the rheumatic diseases.
AU Matteson E.L.
CS Dr. E.L. Matteson, Division of Rheumatology, Department of Internal Medicine, Mayo Clinic Graduate School Medicine, Rochester, MN 55905, United States
SO Current Opinion in Rheumatology, (1997) 9/2 (95-101).
Refs: 49
ISSN: 1040-8711 CODEN: CORHES
CY United States
DT Journal
FS 031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB This paper reviews clinical trials that have been published during the course of the past year on the rheumatologic diseases. The greatest number of clinical trials were done in rheumatoid arthritis. These trials show promising results for combination therapy with disease-modifying antirheumatic drugs, whereas results of studies with **monoclonal** antilymphocyte antibodies have been disappointing. The role of oral collagen remains to be defined. Nonsteroidal anti-inflammatory drugs with selective cyclooxygenase-2 (Cox-2) **inhibition** may have a more favorable

toxicity profile and are likely to find wide use. As adjuvant therapy, trimethoprim-sulfamethoxazole appears to be useful in preventing relapses in Wegener's granulomatosis, and patients develop fewer infections. With the exception of juvenile rheumatoid arthritis, intravenous **immunoglobulin therapy** appeared ineffective in the diseases studied. The inclusion of more standardized and disease-specific outcome measures has enhanced the quality of clinical trials in rheumatology and their applicability to rheumatologic practice.

L31 ANSWER 6 OF 28 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 97-38897 DRUGU P
TI Maximising the therapeutic window of the anti-carcinoma single-chain immunotoxin **BR96** sFv-PE40.
AU Siegall C B; Chace D; Mixan B; Sugai J; Linsley P S; Haggerty H; Warner G; Davidson T
CS Bristol-Squibb
LO Seattle, Wash.; Syracruse, N.Y., USA
SO Proc.Am.Assoc.Cancer Res. (38, 88 Meet., 28, 1997) ISSN: 0197-016X
AV Bristol-Myers Squibb, Pharmaceutical Reseach Inst., Seattle, WA 98121, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 97-38897 DRUGU P
AB Immunogenicity and vascular leak syndrome are the most limiting **toxicities** of the single-chain immunotoxin **BR96** sFv-PE40, which binds to the **Ley** antigen. **BR96** sFv-PE40 is a potent antitumor agent that has been shown to cure established human carcinoma xenografts implanted in mice and rats, and is currently being evaluated in a phase I clinical trial. Administration of **BR96** sFv-PE40 with either deoxyspergualin, dexamethasone or CTLA-4 **Ig**, caused a reduction of antiimmunotoxin Ab's which were able to induce rapid clearance of the immunotoxin and potential kidney **toxicities**. Prophylactic administration of antiinflammatory agents including NSAIDs, dexamethasone, and PLA2 **inhibitors**, was found to **inhibit BR96** sFv-PE40 induced VLS. (conference abstract).
ABEX **BR96** sFv-PE40 was immunogenic in mice, rats, and dogs by approximately 10 days post-administration. Concomitant administration of **BR96** sFv-PE40 and the immunosuppressive agents deoxyspergualin, dexamethasone, or CTLA4-**Ig** resulted in a reduction of antiimmunotoxin Ab's which were able to induce rapid clearance of the immunotoxin and potential kidney **toxicities**. Using rats, in which high-dose **BR96** sFv-PE40 induces VLS and pulmonary edema, prophylactic

administration of antiinflammatory agents including NSAIDs, dexamethasone, and PLA2 **inhibitors**, was found to **inhibit** VLS. Combination therapy of **BR96** sFv-PE40 and the chemotherapeutic agent paclitaxel were found to induce greater antitumor affects in rodents carrying large tumor burdens than either agent alone, and without increasing overall **toxicity**. (RPG)

L31 ANSWER 7 OF 28 MEDLINE DUPLICATE 3
AN 96420258 MEDLINE
DN 96420258
TI Anti-graft-versus-host disease effect of DT390-anti-CD3sFv, a single-chain Fv fusion immunotoxin specifically targeting the CD3 epsilon moiety of the T-cell receptor.
AU Vallera D A; Panoskaltsis-Mortari A; Jost C; Ramakrishnan S; Eide C R; Kreitman R J; Nicholls P J; Pennell C; Blazar B R
CS Department of Therapeutic Radiology, University of Minnesota Hospital and Clinics, Minneapolis 55455, USA.
NC PO1-CA21737 (NCI)
RO1-AI34495 (NIAID)
RO1-CA36725 (NCI)
+
SO BLOOD, (1996 Sep 15) 88 (6) 2342-53.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199612
AB In a recent study, we showed that an immunotoxin (IT) made with a conventional **monoclonal** antibody targeting the CD3 epsilon moiety of the T-cell receptor (TCR) had a potent, but partial, graft-versus-host disease (GVHD) effect (Vallera et al, Blood 86:4367, 1995). Therefore, in this current study, we determined whether a fusion immunotoxin made with anti-CD3 single-chain Fv (sFv), the smallest unit of antibody recognizing antigen, would have anti-GVHD activity. A fusion protein was synthesized from a construct made by splicing sFv cDNA from the **hybridoma** 145-2C11 to a truncated form of the diphtheria toxin (DT390) gene. DT390 encodes a molecule that retains full enzymatic activity, but excludes the native DT binding domain. The DT390-anti-CD3sFv hybrid gene was cloned into a vector under the control of an inducible promoter. The protein was expressed in Escherichia coli and then purified from inclusion bodies. The DT390 moiety of the protein had full enzymatic activity compared with native DT and DT390-anti-CD3sFv, with an IC50 of 1 to 2 nmol/L against phytohemagglutinin-stimulated and alloantigen-stimulated T cells. Specificity was shown (1) by blocking the IT with parental anti-CD3 antibody, but not with a control antibody; (2) by failure of

DT390-anti-CD3sFv to **inhibit** lipopolysaccharide-stimulated murine B cells; (3) by failure of an **Ig** control fusion protein, DT390-Fc, to **inhibit** T-cell responses; and (4) with in vivo immunohistochemisty studies. GVHD was studied in a model in which C57BL/6 (H-2b)-purified lymph node T cells were **administered** to major histocompatibility complex (MHC) antigen disparate unirradiated C.B.-17 scid (H-2d) mice to assess GVHD effects in the absence of irradiation **toxicity**. Flow cytometry studies showed that donor T cells were expanded 57-fold and histopathologic analysis showed the hallmarks of a lethal model of GVHD. Control mice receiving phosphate-buffered saline showed 17% survival on day 80 after bone marrow transplantation, and mice receiving 2 micrograms DT390-Fc fusion toxin control **administered** in 2 daily doses for 6 days (days 0 through 5) had a 43% survival rate. In contrast, 86% of mice receiving the same dose of DT390-anti-CD3sFv were survivors on day 80, a significant improvement, although survivors still showed histopathologic signs of GVHD. These findings suggest that new anti-GVHD agents can be genetically engineered and warrant further investigation of fusion proteins for GVHD treatment.

L31 ANSWER 8 OF 28 MEDLINE DUPLICATE 4
AN 96191015 MEDLINE
DN 96191015
TI Short course single agent therapy with an LFA-3-IgG1 fusion protein prolongs primate cardiac allograft survival.
AU Kaplon R J; Hochman P S; Michler R E; Kwiatkowski P A; Edwards N M; Berger C L; Xu H; Meier W; Wallner B P; Chisholm P; Marboe C C
CS Department of Surgery, College of Physicians and Surgeons, Columbia University, New York, New York 10032, USA.
SO TRANSPLANTATION, (1996 Feb 15) 61 (3) 356-63.
Journal code: WEJ. ISSN: 0041-1337.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199608
AB The interaction of T cell costimulatory molecules with their ligands is required for optimal T cell activation. Interference with such interactions can induce antigen unresponsiveness and delay xeno- and allograft rejection. We have previously shown that LFA3TIP, a soluble human lymphocyte function-associated antigen (LFA)-3 construct, binds CD2 and **inhibits** responses of human T cells in vitro. This study reports the first use of a human fusion protein, LFA3TIP, to significantly prolong primate cardiac allograft survival. Based on our observations that LFA3TIP **inhibits** baboon allogeneic mixed lymphocyte reactions, we gave baboon recipients of heterotopic cardiac allografts injections of LFA3TIP, 3 mg/kg i.v., for 12 consecutive days, starting 2 days before

transplantation. This regimen delayed graft rejection from an average of 10.6 +/- 2.3 days for human **IgG**-treated controls (n = 5) to an average of 18.0 +/- 5.3 days for LFA3TIP-injected animals (n = 7; P < or = 0.01). Grafts from LFA3TIP-treated animals showed markedly diminished coronary endothelialitis as compared with control animals. LFA3TIP reached peak serum levels of approximately 100 micrograms/ml after 7-9 injections and persisted in the 10-micrograms/ml range for 1 to 2 weeks after the final injection. Despite these blood levels, circulating antibodies to LFA3TIP were not detected in the serum. No renal or hepatic **toxicity** was noted. The possible mechanism by which LFA3TIP acts to **inhibit** graft rejection is discussed; success in prolonging graft survival when LFA3TIP is used as a single-agent therapy suggests great potential for this novel therapeutic agent.

L31 ANSWER 9 OF 28 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.
AN 95259508 EMBASE
TI Inhibition of lymphoma growth in vivo by combined treatment with hydroxyethyl starch deferoxamine conjugate and IgG **monoclonal** antibodies against the transferrin receptor.
AU Kemp J.D.; Cardillo T.; Stewart B.C.; Kehrberg E.; Weiner G.; Hedlund B.; Naumann P.W.
CS 5238 Carver, University of Iowa Hospitals, Iowa City, IA 52242, United States
SO Cancer Research, (1995) 55/17 (3817-3824).
ISSN: 0008-5472 CODEN: CNREA8
CY United States
DT Journal
FS 016 Cancer
025 Hematology
037 Drug Literature Index
LA English
SL English
AB Synergistic **inhibition** of hematopoietic tumor growth can be observed in vitro when the iron chelator deferoxamine (DFO) is used in combination with an **IgG mAb** against the anti-transferrin receptor antibody (ATRA). Our goal was to ascertain whether similar findings could be seen in vivo. A high molecular weight conjugate of deferoxamine, known as hydroxyethyl starch (HES) DFO or HES-DFO, was tested in conjunction with C2, a well-defined rat antimouse transferrin receptor **mAb**, against the 38C13 tumor in C3H/HeN mice. It was shown that while neither HES-DFO alone nor C2 alone produced consistent, significant **inhibition** of tumor growth, the combination of HES- DFO and C2 produced virtually complete **inhibition** of initial tumor outgrowth. The latter combination failed, however, to **inhibit** the growth of established tumors. It was then found that when C2 was used in conjunction with RL34, another **IgG** ATRA, the two

ATRAS were themselves capable of causing synergistic **inhibition** of the growth of 38C13 in vitro. When the two **IgG** ATRAS were used together in vivo, regressions of established tumors were observed. Moreover, the addition of HES-DFO to the **IgG** ATRA pair then caused more frequent regressions. Although there was never any obvious **toxicity** seen with a single **IgG** ATRA, the use of the **IgG** ATRA pair was associated with sporadic mortality. In addition, although HES-DFO by itself was also not associated with any obvious **toxicity**, combined treatment with HES-DFO and a single ATRA resulted in death due to bacterial infection in about half of the mice after 10-15 days. Combined treatment with HES-DFO and the ATRA pair resulted in death attributed to infection in nearly all of the mice after 6 days. Thus, an iron deprivation treatment protocol with HES-DFO and **IgG** ATRAS produced both a significant antitumor effect and an increased risk of infection in a taurine model system.

L31 ANSWER 10 OF 28 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.DUPLICATE 5

AN 95346573 EMBASE

TI In vivo cytotoxicity of **monoclonal** antibody-carboplatin immunoconjugates and tissue platinum distribution in tumor-bearing nude mice.

AU Takeda A.; Miyoshi T.; Isono K.

CS Department of Surgery, Yokohama Rosai Hospital, 3231 Kozukue-cho, Kohoku-ku, Yokohama 222, Japan

SO Biotherapy, (1995) 9/10 (1253-1257).
ISSN: 0914-2223 CODEN: BITPE

CY Japan

DT Journal

FS 016 Cancer
026 Immunology, Serology and Transplantation
037 Drug Literature Index

LA Japanese

SL English; Japanese

AB In vivo anti-tumor effect of **monoclonal** antibody (1B2) carboplatin conjugates (immunoconjugates) and tissue platinum distribution were evaluated in nude mice bearing human ovarian cancer. Animals given immunoconjugates showed significantly stronger tumor growth suppression than those given the same dose drug alone, antibodies alone, or nonspecific mouse **IgG** drug conjugates. Thirty minutes later, after **administration**, platinum accumulation in the tumor was significantly higher in the CBDCA-conjugates group than in the other group. Almost similar results were obtained two or twenty four hours later. But serum platinum concentrations of a lower level were observed in every experimental group. We conclude that **immunotargeting therapy** guided CBDCA-conjugates reduced the systemic

toxicity of the drug and induced an earlier **inhibition** of tumor growth.

L31 ANSWER 11 OF 28 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.
AN 96019838 EMBASE
TI Therapy and imaging of pancreatic carcinoma xenografts with radioiodine-labeled chimeric **monoclonal** antibody A10 and its Fab fragment.
AU Kamigaki T.; Yamamoto M.; Ohyanagi H.; Ohya M.; Shimazoe T.; Kono A.; Ohtani W.; Narita Y.; Ohkubo M.; Saitoh Y.
CS First Department of Surgery, Kobe University School of Medicine, 7-5-2 Kusunoki-cho, Chuo-ku, Kobe 650, Japan
SO Japanese Journal of Cancer Research, (1995) 86/12 (1216-1223). ISSN: 0910-5050 CODEN: JJCREP
CY Japan
DT Journal
FS 016 Cancer
023 Nuclear Medicine
026 Immunology, Serology and Transplantation
048 Gastroenterology
037 Drug Literature Index
LA English
SL English
AB Recombinant mouse/human chimeric **monoclonal** antibody A10 (ch-A10) and its Fab fragment (ch-Fab) react with carcinoembryonic antigen on various gastrointestinal carcinomas. We performed biodistribution studies with 125I-labeled ch-A10 and ch-Fab in an antigen-positive human pancreatic carcinoma (BxPC-3) xenograft model. We also evaluated the anti-tumor effect of 131I-labeled ch-A10 and studied the detection of BxPC-3 xenografts with 123I-labeled ch-Fab in whole body scintigraphy. In comparative biodistribution studies, the tumor uptake of 125I-labeled ch-A10 was significantly greater than that of 125I-labeled ch-Fab 24 h post-injection. However, the tumor-to-blood ratio was 46.8 for ch-Fab at 24 h post-injection, while it was only 1.4 for ch-A10. Microautoradiography studies showed that ch-Fab penetrated more uniformly into the tumor nodules than did ch-A10. In mice given a therapeutic dose of 131I-labeled ch-A10, a significant **inhibition** of tumor growth was seen, while control 131I-labeled human **IgG** did not affect tumor growth. Leukocyte **toxicity** was observed within 3 weeks after injection of 131I-labeled ch-A10, but leukocyte counts recovered to normal levels at 8 weeks post-injection. In whole-body scintigraphy, clear and rapid tumor imaging was obtained with 200 .mu.Ci of 123I-labeled ch-Fab 24 h post-injection. These results suggest that radioiodine-labeled chimeric A10 antibodies could potentially be useful candidates for radioimmunotherapy and radioimmunodetection of pancreatic carcinomas.

L31 ANSWER 12 OF 28 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.
AN 94244558 EMBASE
TI Mechanisms of endothelial cell injury in vasculitis.
AU Pall A.A.; Savage C.O.S.
CS Medical School, Department of Medicine, University of Birmingham, Edgbaston, Birmingham B15 2TT, United Kingdom
SO SPRINGER SEMIN. IMMUNOPATHOL., (1994) 16/1 (23-37).
ISSN: 0344-4325 CODEN: SSIMDV
CY Germany, Federal Republic of
DT Journal
FS 005 General Pathology and Pathological Anatomy
025 Hematology
026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
037 Drug Literature Index
LA English
SL English
AB The aetiology of the primary systemic vasculitides remains obscure. Recent years have seen significant advances in our understanding of inflammation and in particular the role of and interaction between the vascular endothelium, mediators and immune effector cells. This has helped to further elucidate those specific processes relevant to vasculitis which result in endothelial cell damage. In Wegener's granulomatosis and microscopic polyarteritis the evidence favours an autoimmune inflammatory response characterised by specific mediators in which the endothelium is both target and active participant current treatment of these disorders with combinations of corticosteroids and cytotoxics is highly effective in inducing remission. However, long-term use of this therapy is potentially **toxic** and there remains also a significant risk of relapse. It is hoped that increased understanding of the pathogenesis of systemic vasculitis will enable more specific, less **toxic** and more effective therapies to be defined. Jayne et al. have suggested a beneficial effect of intravenous pooled normal human **immunoglobulin** (IVIG) in patients with ANCA-positive vasculitis. In vitro studies have shown that IVIG contains antiidiotypic antibodies to NACA and AECA, capable of **inhibiting** the binding of these autoantibodies to their autoantigens. In vivo, IVIG may also provide the immunoregulatory elements needed for the idiotype network and control of the autoimmune repertoire. Mathieson et al. successfully used **monoclonal** antibodies to T cells (Campath-H directed against CDw52) in a patient with ANCA-negative dermal lymphocytic vasculitis. **Monoclonal** antibodies to CAMs have been used in human renal transplant rejection and reduced the inflammation and proteinuria in animal models of anti-glomerular basement membrane disease. In vasculitis, the therapeutic use of specific anti-CAM antibodies may result from further definition of the role of CAMs. Increased understanding of the pathogenesis of systemic vasculitis

is likely to provide the basis for the use of more specific **immunotherapies** in the future.

L31 ANSWER 13 OF 28 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.
AN 94146767 EMBASE
TI New developments in the treatment of systemic vasculitis.
AU Gross W.L.
CS DIMCI, Rheumaklinik Bad Bramstedt, 24572 Bad Bramstedt, Germany, Federal Republic of
SO CURR. OPIN. RHEUMATOL., (1994) 6/1 (11-19).
ISSN: 1040-8711 CODEN: CORHES
CY United States
DT Journal
FS 006 Internal Medicine
026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Although precise diagnosis of the systemic vasculitides can provide general prognostic information and help to guide initial therapy, recent studies on the long-term clinical course have revealed considerable variation in clinical severity. Therefore, anatomic distribution of involvement and speed of progression should be the principle determinants of the intensity of **immunosuppressive therapy**. In progressive pulmonary or renal disease, eg, Wegener's granulomatosis, aggressive 'standard' therapy is obligatory, eg, daily cyclophosphamide and glucocorticoids. Such regimens, however, should be applied with caution in chronic or indolent and abortive forms of systemic vasculitis, because follow-up studies (eg, in Wegener's granulomatosis) have revealed treatment-associated morbidity rates of up to 42%, disease-related morbidity, and a high incidence of relapse under treatment. Moreover, less **toxic** therapeutic strategies are being pursued with remarkable success: low- dose weekly methotrexate, monthly intravenous or oral pulses of cyclophosphamide plus glucocorticoids, and high-dose intravenous **immunoglobulin**. Long-term remission of intractable (non-antineutrophil cytoplasmic antibody-associated) systemic vasculitis has been achieved using humanized **monoclonal** antibodies (ie, anti-CD4/anti-CDw52); and amelioration of glomerulonephritis in immune complex diseases (eg, systemic lupus erythematosus) has been achieved with nafamostat mesilate, an **inhibitor** of complement serine proteases. In addition, leukocytoclastic vasculitis has been effectively controlled with pentoxifylline, presumably by neutralizing proinflammatory cytokines, and hepatitis C virus-associated mixed cryoglobulinemia has been successfully treated with interferon alfa.

L31 ANSWER 14 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 6
AN 93:230647 BIOSIS
DN BA95:121822
TI **LE**-GAMMA SPECIFIC ANTIBODY WITH POTENT ANTI-TUMOR ACTIVITY IS INTERNALIZED AND DEGRADED IN LYSOSOMES.
AU GARRIGUES J; GARRIGUES U; HELLSTOM I; HELLSTROM K E
CS BRISTOL-MYERS SQUIBB COMPANY, 3005 FIRST AVENUE, SEATTLE, WA 98121.
SO AM J PATHOL 142 (2). 1993. 607-622. CODEN: AJPAA4 ISSN: 0002-9440
LA English
AB **BR96** is a **monoclonal** antibody (**MAb**) that recognizes many human carcinomas and can kill antigen-positive tumor cells in vitro. Using both gold and radiolabeled **MAb**, the distribution and cellular processing of **BR96** during cytolysis has been determined. After a brief (< 3 minutes) **MAb** treatment, cells in suspension are stained by the nuclear viability dye propidium iodide. Whole **MAb** and F(ab')2 fragments are equally cytotoxic; monovalent F(ab) fragments, however, have no effect on dye uptake unless cross-linked with goat anti-mouse **IgG**. The level of **toxicity** is dependent on both **MAb** dose and on cell surface receptor density. Cell contact may regulate receptor expression. **BR96** receptors are more abundant on cells migrating into the open areas of a scratch wounded confluent culture than on the adjacent contact-**inhibited** cells. **BR96** can also **inhibit** the anchorage-independent growth of tumor cells in soft agar showing that its effects on propidium iodide staining are not due to transient changes in membrane permeability. Immunogold electron microscopy reveals that, after a 1-minute treatment, **BR96** induces significant infolding of the plasma membrane and that internalized **MAb** is localized to these structures. Immediately thereafter, large cell surface and intracellular vesicles form, mitochondria are swollen, and membrane integrity is lost. Therefore, **BR96** seems to cause morphological changes characteristic of necrosis rather than apoptosis. When bound to adherent carcinoma cells, **BR96** is distributed uniformally on the apical surface of cells labeled at 4 C and is enriched at points of cell substratum contact. Upon warming of the cells to 37 C, **BR96** localizes in small perinuclear clusters and the cell margin is now devoid of label. Immunogold electron microscopy reveals that **BR96** undergoes receptor mediated internalization and is localized within the same coated pits, endosomes, and lysosomes as the transferrin receptor. Quantitative studies using iodinated **BR96** show that after 6 hours of chase, a maximum of 53% of the radiolabel is located within the intracellular pool. Analysis by sodium dodecyl sulfate-polyacrylamide gel electrophoresis indicates that 84% of this fraction is nondegraded. **BR96** probably cycles between the medium and intracellular pools because the remainder of the radiolabel is in the medium as intact **MAb**. By 24 hours of chase, the intracellular fraction drops to 30%, while

the remaining 70% is present in the culture medium, mostly as low molecular weight degradation products.

L31 ANSWER 15 OF 28 PROMT COPYRIGHT 1998 IAC

AN 93:557033 PROMT
TI Phase I Trial of Anti-Idiotypic Antibody Vaccine Melimmune-2 TM in Patients with Resected Poor Risk Malignant Melanoma
SO Cancer Weekly, (22 Mar 1993) pp. N/A.
LA English
WC 358
FULL TEXT IS AVAILABLE IN THE ALL FORMAT
AB AUTHORS: J.L. Murray, R.W. Carlson, K.M. Adler, H. Brewer, L. Bendon, S. Raychaudhuri and J. Merritt. University of Texas M.D. Anderson Cancer Center, Houston, Texas; Stanford University, Stanford, California, and IDEC Pharmaceuticals, LaJolla, California. According to an abstract presented by the authors to the Specific **Immunotherapy** of Cancer Vaccines Conference, held January 21-24, 1993, in Washington, D.C., "The anti -idiotypic Murine **monoclonal** antibody Melimmune-2(TM) (Ab(2)) is a surrogate antigen for the higher molecular weight proteoglycan (MPG) expressed by >80% of human malignant melanoma. We performed a Phase I trial in 13 melanoma patients with resected AJCC Stage II, III or IV disease to determine **toxicity**, optimal dosing schedule and immunologic response. Melimmune-2 (2 mg) was mixed with either 100 or 200 ug of novel adjuvant SAF-m and **administered** as either a single i.m. injection (100 ug SAF-m/inj; 7 pts) or two split injections at separate sites (100 ug SAF-m/inj; 6 pts) every 2 weeks x 4, followed by every 8 weeks x 2 for a total of 6 vaccinations. Sera were collected for measurement of total immune response; Ab(3) was determined by direct binding to Melimmune-2 (HAMA depleted serum) as well as by **inhibition** RIA. **Toxicity** was not dependent on SAF-m dose or numbers of injections and consisted of local erythema and induration at the injection site along with fever, headaches and myalgias. Two patients developed moderately severe fever and arthralgias; one of the two had a self-limited episode of low grade asymptomatic anterior uveitis. Both had been PPD(+) prior to study. HAMA to Melimmune-2 antibodies (total response) were measured in all patients; titers ranged from 1:128 to 1:8192. **IgG** anti-anti-idiotype antibodies were detected in all patients (range; 1:20 to 1:1000) and increased as a result of repeated immunizations. Affinity-purified Ab(3) bound to MPG in an RIA, and immunoprecipitated the 400 and 25 kD forms of MPG from a melanoma cell line. Four patients have recurred to date; there was no correlation between disease free interval and development of total HAMA or Ab(3) titers. In summary, Melimmune-2 + SAF-m is safe and immunogenic at the above doses and schedule. Single site immunization appears as efficacious as split dosing."

Searcher : Shears 308-4994

L31 ANSWER 16 OF 28 CANCERLIT
AN 92686024 CANCERLIT
DN 92686024
TI IMMUNOTOXINS.
AU Spitler L E
CS Northern California Melanoma Center, San Francisco, CA.
SO Non-serial, (1991). Principles of Cancer Biotherapy. Second Edition. Oldham RK, ed. New York, Marcel Dekker, p. 433-56, 1991.
DT Book; (MONOGRAPH)
(REVIEW, ACADEMIC)
General Review; (REVIEW)
FS ICDB
LA English
EM 199211
AB Immunotoxins consist of a **monoclonal** antibody (**MAb**) or other targeting agent conjugated to a toxin that can kill cells. The term 'immunotoxin' generally has been reserved for conjugates in which the **toxic** moiety is a ribosomal-**inhibiting** protein. Such proteins occur naturally in a variety of bacteria, plants and animals. Preclinical studies, clinical trials and issues related to **immunotoxin therapy** are reviewed. Topics include in vivo and in vitro studies; clinical results (melanoma, breast cancer, colorectal cancer, leukemia/lymphoma, ovarian cancer and graft-vs-host disease [GvHD]); and questions for second-generation studies (stability of conjugates in vivo, cellular heterogeneity, access and localization in tumor, biodistribution, immune response and potentiators). Preclinical and clinical studies have shown clearly the potential of immunotoxins for targeted therapy. Immunotoxins can be **administered** safely, and side effects from the ricin A-chain component are transient and well tolerated. Severe **toxicity** can result if the **MAb** has unrecognized cross-reactivity with normal tissues and targets the toxin inappropriately to an unwanted target. There is an immune response to both the murine **Ig** and toxin components of immunotoxin, except in some patients with leukemia and lymphoma, which precludes repeated courses of treatment. Encouraging results in lymphomas, leukemias and GvHD suggest that it is possible to achieve efficacy following in vivo **administration** of immunotoxin. Impressive responses have been observed in patients with solid tumors treated with immunotoxins, but the reasons for these responses are not understood. (108 Refs)

L31 ANSWER 17 OF 28 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.
AN 91313489 EMBASE
TI Immunotoxins constructed with anti-CD25 **monoclonal** antibodies and deglycosylated ricin A-chain have potent anti-tumour

effects against human Hodgkin cells in vitro and solid Hodgkin tumours in mice.

AU Engert A.; Martin G.; Amlot P.; Wijdenes J.; Diehl V.; Thorpe P.

CS Cancer Immunobiology Center, University of Texas Southwestern, 5323 Harry Hines Blvd., Dallas, TX 75235, United States

SO INT. J. CANCER, (1991) 49/3 (450-456).
ISSN: 0020-7136 CODEN: IJCNAW

CY United States

DT Journal

FS 016 Cancer
026 Immunology, Serology and Transplantation
037 Drug Literature Index

LA English

AB Twenty-three **monoclonal** antibodies (**MAbs**) against the IL-2 receptor .alpha.-chain (CD25) were evaluated as ricin A-chain immunotoxins for the treatment of Hodgkin's disease. Primary screening used an indirect assay in which the cells were treated with the test antibody followed by Fab' immunotoxin against mouse **immunoglobulin**. This screening identified 5 **MAbs** which **inhibited** protein synthesis in L540 Hodgkin cells by 50% at a concentration (IC50) of 6 x 10-11 M or less: RFT5.gamma.1, RFT5.gamma.2a, B-B10, B-F2 and B-G3. These **MAbs** were then linked directly to deglycosylated ricin A-chain (dgA) and were confirmed to have potent and specific **toxicity** for L540 cells. The immunotoxins had the following potency order: RFT5.gamma.1 > RFT5.gamma.2a > B-B10 > B-F2 > B-G3. The most effective immunotoxin, RFT5.gamma.1.cntdot.dgA, had an IC50 value of 7 x 10-12 M, which is the same as that of whole ricin. In vivo, a single intravenous injection of 48 .mu.g of RFT5.gamma.1.cntdot.dgA, RFT5.gamma.2a.cntdot.dgA, B-B10.cntdot.dgA or B-F2 induced lasting complete remissions in 78, 66, 50 and 44%, respectively, of nude mice bearing subcutaneous solid L540 tumours of 0.7 cm diameter. Two tumours which regrew after B-B10.cntdot.dgA treatment were re-established in tissue culture. Both had reduced sensitivity to B-B10.cntdot.dgA in vitro but not to immunotoxins recognizing different antigens on Hodgkin cells. The **MAbs** that produced the most potent immunotoxins, RFT5.gamma.1, RFT5.gamma.2a and B-B10, had no significant cross-reactivity with normal human tissues outside the lymphoid system as judged from indirect immunoperoxidase staining of frozen sections. By contrast, B-F2 strongly stained normal human renal tubules.

L31 ANSWER 18 OF 28 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 7

AN 91:72157 BIOSIS

DN BA91:40817

TI ACTIVE SPECIFIC **IMMUNOTHERAPY** IN PATIENTS WITH MELANOMA A CLINICAL TRIAL WITH MOUSE ANTIIDIOTYPIC **MONOCLONAL** ANTIBODIES ELICITED WITH SYNGENEIC ANTI-HIGH-MOLECULAR-WEIGHT-MELANOMA-ASSOCIATED ANTIGEN **MONOCLONAL** ANTIBODIES.

Searcher : Shears 308-4994

AU MITTELMAN A; CHEN Z J; KAGESHITA T; YANG H; YAMADA M; BASKIND P; GOLDBERG N; PUCCIO C; AHMED T; ARLIN Z; FERRONE S
CS NEW YORK MED. COLL., VALHALLA, NY 10595.
SO J CLIN INVEST 86 (6). 1990. 2136-2144. CODEN: JCINAO ISSN: 0021-9738
LA English
AB In two clinical trials the mouse antiidiotypic **monoclonal** antibody (**MAb**) MF11-30, which bears the internal image of human high-molecular-weight-melanoma-associated antigen (HMW-MAA) was **administered** by subcutaneous route without adjuvants to patients with stage IV malignant melanoma on day 0, 7, and 28. Additional injections were **administered** if anti-antiidiotypic antibodies were not found or their titer decreased. In the first phase I trial with 16 patients the initial dose was 0.5 mg per injection and escalated to 4 mg per injection. Neither **toxicity** nor allergic reactions were observed despite the development of anti-mouse **Ig** antibodies. Minor responses were observed in three patients. In a second clinical trial **MAb** MF11-30 was **administered** to 21 patients at a dose of 2 mg per injection, since this dose had been shown in the initial study to be effective in inducing anti-antiidiotypic antibodies. Two patients were inevaluable; in the remaining 19 patients, the average duration of treatment was 34 wk. In this trial as well, neither **toxicity** nor allergic reactions were observed. 17 of the 19 immunized patients increased the levels of anti-mouse **Ig** antibodies and 16 developed antibodies that **inhibit** the binding of antiidiotypic **MAb** MF11-30 to the immunizing anti-HMW-MAA **MAb** 225.28. One patient increased the level of anti-HMW-MAA antibodies. One patient achieved a complete remission with disappearance of multiple abdominal lymph nodes for a duration of 95 wk. Minor responses were observed in three patients. These results suggest that mouse antiidiotypic **MAb** that bear the internal image of HMW-MAA may be useful reagents to implement active specific **immunotherapy** in patients with melanoma.

L31 ANSWER 19 OF 28 BIOTECHDS COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 89-05127 BIOTECHDS
TI **Immunotoxin therapies** using ricin-A chain; and mouse or human **monoclonal** antibody
PA Xoma
PI WO 8900583 26 Jan 1989
AI WO 88-US2343 12 Jul 1988
PRAI US 87-74824 17 Jul 1987
DT Patent
LA English
OS WPI: 89-054070 [07]
AN 89-05127 BIOTECHDS
AB A new method for **inhibiting** the expansion or activity of a predetermined cell population in a patient involves

administering an effective dose of an immunotoxin preparation comprising a binding component capable of attaching to cells and a ricin-A chain (RTA) complexed with the binding component. The RTA contains at least 75%, preferably 85-95% RTA-30. The RTA-30 species (mol.wt. 30,000) may be purified from ricin with an immunoaffinity column. The binding component is an **immunoglobulin**, preferably a **monoclonal** antibody (**mAb**). Intact **immunoglobulins** or their fragments such as Fv, Fab, F(ab)2, half antibody molecules are used. The preferred **IgM** or **IgG mAbs** are of mouse, human or other mammalian origin. Common sources of **mAbs** are immortalized mouse of human cell lines that may be cloned and screened in accordance with conventional techniques. The new therapy is directed against immune cells, specifically tumor cells or cells from a bone marrow transplant donor.The RTA-30-based immunotoxins can be used to selectively remove harmful cell populations in vivo or extracorporeally with minimal non-specific **toxicity**. (33pp)

L31 ANSWER 20 OF 28 MEDLINE DUPLICATE 8
AN 89275057 MEDLINE
DN 89275057
TI Cytotoxicity against human tumor cells mediated by the conjugate of anti-epidermal growth factor receptor **monoclonal** antibody to recombinant ricin A chain.
AU Masui H; Kamrath H; Apell G; Houston L L; Mendelsohn J
CS Memorial Sloan-Kettering Cancer Center, New York, New York 10021.
NC CA37641 (NCI)
CA42060 (NCI)
SO CANCER RESEARCH, (1989 Jul 1) 49 (13) 3482-8.
Journal code: CNF. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198909
AB We have produced **monoclonal** antibodies against the epidermal growth factor (EGF) receptor which bind to the receptor with high affinity, compete with EGF for binding, block EGF-induced tyrosine kinase activity, and activate internalization and down-regulation of the receptor. These antibodies are cytostatic against cultured A431 cells at concentrations of 5-20 nM. In addition, they prevent the growth of A431 tumor xenografts in athymic mice. In the present experiments, we have attempted to improve the antitumor activity of **monoclonal** antibody 528 IgG2a against the EGF receptor by linking it to recombinant ricin A chain (rRA). The immunoconjugate (528 **IgG**-rRA) showed a potent cytotoxic effect on A431 cells in vitro. At a concentration of 10 pM, it **inhibited** the proliferation of cultured A431

cells by 50% and also **inhibited** protein synthesis in these cells by 50%. Proliferation was prevented and cell death occurred at 528 **IgG**-rRA concentrations of 60 pM or greater. Recombinant free ricin A chain was far less **toxic**. The cytotoxic effect of the immunoconjugate was neutralized by 528 **IgG** at concentrations 100-fold higher than 528 **IgG** -rRA. When the cytotoxic effect of 528 **IgG**-rRA was compared among several human cell lines expressing different numbers of EGF receptors, the capacity to **inhibit** both proliferation and protein synthesis generally correlated with the number of EGF receptors on the plasma membranes of these cells. Since 528 **IgG**-rRA is a very potent immunotoxin against A431 cells in culture, we designed experiments to test its in vivo antitumor activity against A431 xenografts in athymic mice. To measure the clearance of 528 **IgG**-rRA, 50 micrograms of immunotoxin were injected i.p. into athymic mice, blood was collected from the animals at regular intervals, and the level of immunotoxin in the serum was assayed by protein synthesis **inhibition** in cultured A431 cells. The blood level of active immunoconjugate reached a maximum 6 h after i.p. injection. The half-life of the absorption phase was 2.2 h, the half-life for elimination was 9.2 h, and blood levels which could be potentially cytotoxic were maintained for 48-72 h. We investigated a number of immunotoxin treatment schedules, including every other day for 4 days, based on these data. The results demonstrate that, while 528 **IgG**-rRA has higher in vivo antitumor activity than 528 **IgG** against A431 cell xenografts, this is accompanied by **toxicity** against the murine host.

L31 ANSWER 21 OF 28 MEDLINE DUPLICATE 9
AN 88210325 MEDLINE
DN 88210325
TI Radioimmunotherapy of human colonic cancer xenografts with 90Y labeled **monoclonal** antibodies to carcinoembryonic antigen [published erratum appears in Cancer Res 1988 Aug 15;48(16):4716].
AU Sharkey R M; Kaltovich F A; Shih L B; Fand I; Govelitz G; Goldenberg D M
CS Center for Molecular Medicine and Immunology, Newark, New Jersey 07103.
NC CA 37218 (NCI)
CA 43455 (NCI)
CA 39841 (NCI)
SO CANCER RESEARCH, (1988 Jun 1) 48 (11) 3270-5.
Journal code: CNF. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198808

Searcher : Shears 308-4994

AB **Monoclonal** antibodies (**MAbs**) to carcinoembryonic antigen (CEA) or alpha-fetoprotein (AFP) were conjugated with diethylenetriaminepentaacetic acid and radiolabeled with 90Y at a specific activity of 4.0-6.0 mCi/mg. Approximately 50% of the radiolabeled anti-CEA antibody (90Y-labeled NP-2) bound to an immunoadsorbent containing CEA while analysis by high performance liquid chromatography revealed that 95-98% of the 90Y was associated with **immunoglobulin**. Less than 5% of the 90Y dissociated from either **MAb** after incubation in plasma for 48 h at 37 degrees C. After injection into nude mice, 98% of the circulating radioactivity remained associated with antibody and no loss of immunoreactivity was observed at 3 days. To evaluate 90Y-labeled NP-2 as a therapeutic agent, varied doses (10-100 microCi) were **administered** as a single i.v. injection into groups of nude mice bearing s.c. implants (0.3-0.4 g) of a CEA-producing human colonic cancer xenograft, GW-39. At the 10-microCi dose, no **inhibition** of tumor growth was observed. After 28 days, tumor growth was **inhibited** by as much as 77% in mice treated with 50 microCi of 90Y-labeled NP-2 as compared to tumor growth in control animals given 90Y-labeled anti-AFP. Doses higher than 50 microCi (75 and 100 microCi) were **toxic** to most of the animals, killing them within 2-3 weeks after **administration**. Marked suppression of circulating leukocytes was observed with 20 and 50 microCi by 1-2 weeks postinjection, but they returned to normal levels 3-4 weeks later. These studies show that treatment with 90Y-labeled **MAbs** against CEA can produce significant antitumor effects. However, **toxicity** to the bone marrow may limit the therapeutic efficacy of systemically **administered** 90Y-labeled **MAbs**.

L31 ANSWER 22 OF 28 MEDLINE DUPLICATE 10
AN 88012025 MEDLINE
DN 88012025
TI Biodistribution of antibodies after intraperitoneal or intravenous injection and effect of carbohydrate modifications.
AU Mattes M J
CS Center for Molecular Medicine and Immunology, Newark, NJ 07103..
SO JOURNAL OF THE NATIONAL CANCER INSTITUTE, (1987 Oct) 79 (4) 855-63. Journal code: J9J. ISSN: 0027-8874.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198801
AB These studies were designed to improve the strategy for intraperitoneal **immunotherapy** of human ovarian carcinoma with **monoclonal** antibodies (**MAbs**). Since ovarian tumor cells generally appear to be confined to the peritoneal cavity, regional therapy is appropriate and can reduce the need for

strictly tumor-specific **MAbs**. In normal mice, with the use of radioiodine-labeled **MAbs**, transfer from peritoneal cavity to blood was found to be very rapid, within hours, and this transfer was delayed slightly by increasing the volume injected. The presence of ascitic fluid in mice greatly delayed the rate of transfer. For reduction of possible **toxicity** for normal cells outside the peritoneal cavity, the hepatic receptor for desialylated serum glycoproteins was used. Neuraminidase treatment of all major mouse **immunoglobulin** classes and subclasses, including **IgM**, IgG1, IgG2a, IgG2b, IgG3, and **IgA**, did not cause their rapid blood clearance, although similar treatment of fetuin was effective. Conjugation of **IgG** with galactose, with use of the cyanomethyl derivative, did result in very rapid blood clearance via the hepatic lectin; within 3 minutes clearance was essentially complete. The specificity of uptake was demonstrated by **inhibition** with desialylated fetuin. Degradation within the liver, release of the radioiodine, and excretion from the animal were also quite rapid, within hours. This conjugation procedure had no effect on the antibody activity of the two **MAbs** tested. Such modified **MAbs**, therefore, are degraded almost immediately after entering the blood and would be advantageous in intraperitoneal therapy and in other situations in which regional **immunotherapy** is appropriate.

L31 ANSWER 23 OF 28 MEDLINE DUPLICATE 11
AN 87102608 MEDLINE
DN 87102608
TI Effects of **monoclonal** antibodies that block transferrin receptor function on the in vivo growth of a syngeneic murine leukemia.
AU Sauvage C A; Mendelsohn J C; Lesley J F; Trowbridge I S
NC CA-34787 (NCI)
CA-37641 (NCI)
CA-25893 (NCI)
SO CANCER RESEARCH, (1987 Feb 1) 47 (3) 747-53.
Journal code: CNF. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198705
AB The ability of **monoclonal** antibodies (**MAbs**) against the murine transferrin receptor to **inhibit** the growth of transplanted syngeneic AKR/J SL-2 leukemic cells has been investigated. Two rat **IgM** antibodies, RI7 208 and REM 17.2, which both block transferrin receptor function, **inhibited** the growth of SL-2 leukemic cells in vitro at concentrations of 5-10 micrograms per ml. However, RI7 208 was more effective than REM 17.2 in prolonging survival of tumor-bearing

mice. The antitumor effects of RI7 208 **MAb** were dependent on both the antibody dose and number of leukemic cells inoculated. The serum clearance of [75Se]methionine-labeled RI7 208 and REM 17.2 antibodies was similar and consisted of an initial rapid phase over the first 2 days followed by a slower phase. A single dose of 2 mg of antibody maintained a serum **MAb** concentration (greater than 10 micrograms/ml) sufficient to **inhibit** SL-2 leukemic cell growth in vitro for 2-3 days. The liver, kidney, and spleen were the major sites at which each of the antibodies accumulated regardless of whether trace or saturating amounts of antibody were **administered**. The specific activity of antibody found in s.c. SL-2 tumors was about 2-fold less than that of liver. It was shown that multiple doses of R17 208 **MAb** **administered** on a schedule aimed at maintaining a therapeutic serum level of **MAb** for 1-3 weeks were more effective than a single dose. Further, **administration** of RI7 208 **MAb**, in combination with the anti-Thy-1.1 **MAb** 19E12, was more effective than either antibody alone. SL-2 mutant cells were selected that were resistant to growth **inhibitory** effects of RI7 208 in vitro. The effects of RI7 208 **MAb** on the growth of these mutant cells in vivo suggests the major mechanism by which the **MAb** **inhibits** SL-2 tumor growth is by directly blocking receptor function. Acute **toxicity** associated with **administration** of the **MAb** was minimal. However, assays of myeloid and erythroid colony-forming units in bone marrow and spleen of mice given multiple doses of RI7 208 showed a depression of stem cell activity in bone marrow and elevated numbers of erythroid and cellular colony-forming units in the spleen.

L31 ANSWER 24 OF 28 EMBASE COPYRIGHT 1998 ELSEVIER SCI. B.V.DUPLICATE 12

AN 85061095 EMBASE

TI Human anti-murine immunoglobulin responses in patients receiving **monoclonal** antibody therapy.

AU Schroff R.W.; Foon K.A.; Beatty S.M.; et al.

CS Biological Therapeutics Branch, Biological Response Modifiers Program, National Cancer Institute, Frederick, MD 21701, United States

SO CANCER RES., (1985) 45/2 (879-885).
CODEN: CNREA8

CY United States

LA English

AB Human anti-murine **immunoglobulin** responses were assessed in serum from three groups of patients receiving murine **monoclonal** antibody therapy. Each of the three patient groups responded differently. Chronic lymphocytic leukemia patients demonstrated little or no preexisting murine **immunoglobulin** G-reactive antiglobulin prior to treatment, while the cutaneous

T-cell lymphoma and melanoma patients demonstrated preexisting antiglobulin levels in the same range as those demonstrated in healthy controls. None of 11 chronic lymphocytic leukemia patients receiving the T101 **monoclonal** antibody demonstrated an antiglobulin response, whereas all four of the cutaneous T-cell lymphoma patients receiving the same antibody developed increased levels of antiglobulins. Three of nine malignant melanoma patients receiving the 9.2.27 **monoclonal** antibody showed an increase in antiglobulin titers. In patients developing antiglobulin responses, the response was rapid, typically being detectable within 2 weeks. The antiglobulins were primarily **immunoglobulin** G and, with the exception of a single melanoma patient in whom the response appeared to have a substantial 9.2.27-specific component (i.e., antidiotype), were cross-reactive with most murine **immunoglobulin** G preparations tested. This pattern of results suggested that the antiglobulin was a secondary immume reaction with elevation of the levels of preexisting antiglobulin which was cross-reactive with the mouse antibody **administered**. While the presence of serum antiglobulin would be expected to present major complications to **monoclonal** antibody therapy, no clinical **toxicity** related to antiglobulin responses was observed in these patients, and no **inhibition** of antibody localization on tumor cells was seen.

L31 ANSWER 25 OF 28 CANCERLIT
AN 83608558 CANCERLIT
DN 83608558
TI **MONOCLONAL** ANTIBODY AND AN ANTIBODY-TOXIN CONJUGATE TO A CELL SURFACE PROTEOGLYCAN OF MELANOMA CELLS SUPPRESS IN VIVO TUMOR GROWTH.
AU Bumol T F; Wang Q C; Reisfeld R A; Kaplan N O
CS Dept. Immunology, Scripps Clinic and Res. Foundation, La Jolla, CA, 92037.
SO Proc Natl Acad Sci U S A, (1983). Vol. 80, No. 2, pp. 529-533. ISSN: 0027-8424.
DT Journal; Article; (JOURNAL ARTICLE)
FS ICDB
LA English
EM 198304
AB A **monoclonal** antibody directed against a cell surface chondroitin sulfate proteoglycan of human melanoma cells, 9.2.27, and its diphtheria toxin A chain (DTA) conjugate were investigated for their effects on in vitro protein synthesis and in vivo tumor growth of human melanoma cells. The 9.2.27 **IgG** and its DTA conjugate display similar serological activities against melanoma target cells but only the conjugate can induce consistent in vitro **inhibition** of protein synthesis and **toxicity** in M21 melanoma cells. However, both 9.2.27 **IgG** and its DTA conjugate effects significant suppression of M21 tumor growth in

vivo in an **immunotherapy** model of a rapidly growing tumor in athymic nu/nu mice, suggesting that other host mechanisms may mediate **monoclonal** antibody-induced tumor suppression. (Author abstract) (28 Refs)

L31 ANSWER 26 OF 28 MEDLINE DUPLICATE 13
AN 84106469 MEDLINE
DN 84106469
TI Ricin A-chain conjugated with **monoclonal** anti-L1210 antibody. In vitro and in vivo antitumor activity.
AU Kishida K; Masuho Y; Saito M; Hara T; Fuji H
NC CA26479 (NCI)
SO CANCER IMMUNOLOGY, IMMUNOTHERAPY, (1983) 16 (2) 93-7. Journal code: CN3. ISSN: 0340-7004.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198405
AB In studies of antitumor antibody-cytotoxic agent conjugates as potential antitumor agents with improved tumor specificity, the **toxic** subunit A-chain of ricin was conjugated with a **monoclonal** antibody to a tumor-associated antigen expressed weakly on murine leukemia L1210 cells and strongly on L1210/GZL cells, a guanazole-resistant subline of L1210, employing N-succinimidyl 3-(2-pyridyldithio)propionate as cross-linking agent. The conjugate (anti-L1210 conjugate) exhibited a potent concentration-dependent cytotoxicity against cultured L1210/GZL cells, and **inhibited** cell growth at concentrations over 0.8 micrograms/ml. The conjugate killed all L1210/GZL cells at a concentration of 100 micrograms/ml. Neither nonimmune conjugate similarly prepared from mouse nonimmune **IgG** nor unconjugated anti-L1210 **IgG** alone showed cytotoxicity against L1210/GZL cells. When (BALB/c X DBA/2)F1 mice inoculated with 1 X 10(5) L1210/GZL cells were treated with IP injections of 27 micrograms anti-L1210 conjugate 1 h and 5 days after tumor cell inoculation, a life-prolonging effect was observed. [Lifespan in treated animals as percentage of that in controls (T/C) = 146%]. However, when the dose per injection was increased to 50 micrograms per mouse, survival was the same as in the control group. Postmortem examination of mice that had been treated with 50 micrograms anti-L1210 conjugate revealed lesions with necrosis and hemorrhage in the liver parenchyma and the intestinal epithelium, respectively. A similar **toxic** effect on the host mice was also observed with nonimmune conjugate.

L31 ANSWER 27 OF 28 CANCERLIT
AN 82614600 CANCERLIT
DN 82614600

TI SPECIFIC KILLING OF HUMAN AND MOUSE TUMOR CELLS BY IMMUNOTOXINS.
AU Casellas P; Blythman H E; Brown J P; Gros O; Gros P; Hellstrom K E; Hellstrom I; Jansen F K; Poncelet P; Vidal H
CS Centre de Recherches CLIN MIDY, Monpellier, France.
SO Protides Biol Fluid Proc Colloq, (1982). Vol. 29, pp. 927-932.
DT (MEETING PAPER)
FS ICDB
LA English
EM 198206
AB **Monoclonal** antibodies (anti-Thy 1.2 and anti-human melanoma P97) were used to replace the binding moiety of the B-chain of ricin, in order to obtain immunotoxins that use the purified A-chain of ricin as the **toxic** moiety. The A-chain was coupled to the antibodies via a disulfide linkage, allowing a linkage of active A-chain to antibody ratio of 3:1 for **IgM** anti-Thy 1.2 and 1.4:1 for the **IgG** anti-melanoma immunotoxin. Both immunotoxins showed specific cytotoxicity for their respective target cells. In vitro tests of protein synthesis **inhibition** and of **inhibition** of colony formation demonstrated the specific activity of the immunotoxins. Both immunotoxins could specifically kill the last target cell without damaging control cells, and a specific killing index could be calculated. The loss of binding capacity due to conjugation was estimated to be 10% for anti-Thy 1.2 immunotoxin and 30% for anti-melanoma immunotoxin. (11 Refs)

L31 ANSWER 28 OF 28 CANCERLIT
AN 83601990 CANCERLIT
DN 83601990
TI **MONOCLONAL** ANTI-MM46 ANTIBODY:RICIN A CHAIN CONJUGATE: IN VITRO AND IN VIVO ANTITUMOR ACTIVITY.
AU Seto M; Umemoto N; Saito M; Masuho Y; Hara T; Takahashi T
CS (c/o Hara), Teijin Inst. Biomedical Res., Asahigaoka, Hino, Tokyo 191, Japan.
SO Cancer Res, (1982). Vol. 42, No. 12, pp. 5209-5215.
ISSN: 0008-5472.
DT Journal; Article; (JOURNAL ARTICLE)
FS ICDB
LA English
EM 198302
AB In an approach to antitumor agents with improved tumor specificity, the ricin **toxic** subunit A chain was covalently coupled with a **monoclonal** IgG2b antibody directed against MM antigen, a tumor-specific antigen on syngeneic mouse mammary tumor MM46 cells (anti-MM46 **IgG**), using N-succinimidyl 3-(2-pyridyldithio)propionate as cross-linking agent. The conjugate thus prepared (anti-MM46 conjugate) showed potent dose-dependent cytotoxicity against MM antigen-positive MM46 cells in vitro and **inhibited** the cell growth at concentrations above 1 ug/ml.

The immunological specificity was verified by the observation that anti-MM46 conjugate did not show cytotoxicity against MM antigen-negative MM48 cells. Neither nonimmune conjugate similarly prepared from mouse nonimmune **IgG** nor unconjugated anti-MM46 **IgG** alone exhibited cytotoxicity against MM46 cells. Anti-MM46 **IgG** still retained considerable in vitro complement-dependent cytotoxicity against MM46 cells after conjugation with ricin A chain. In Winn-type tumor-neutralizing assay in which C3H/He mice were inoculated ip or sc with MM46 cells preincubated with a test material, anti-MM46 conjugate showed greater activity than did anti-MM46 **IgG**. A markedly enhanced efficacy of anti-MM46 conjugate was also observed in therapeutic experiments. When a group of five C3H/He mice inoculated ip with 5 x 10(4) MM46 cells were treated with an ip injection of 1 ug of anti-MM46 conjugate on Days 1, 3, and 5, all five mice survived tumor free. The in vivo efficacy of anti-MM46 conjugate over anti-MM46 **IgG** alone was demonstrated by therapeutic experiments as well as by tumor-neutralizing assays. Although anti-MM46 conjugate showed no antitumor effect when injected ip to C3H/He mice bearing sc-inoculated MM46 tumor on Days 1, 3, 5, and 7 at a dose of 10 ug, it **inhibited** tumor growth when injected intraregionally to tumor-bearing mice, suggesting that the conjugate is effective also to solid-type MM46 tumor if a sufficient amount of anti-MM46 conjugate reaches the tumor site. (26 Refs)

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=> d his l32-

     (FILE 'CAPLUS, BIOSIS, MEDLINE, EMBASE, LIFESCI, BIOTECHDS, WPIDS,
     CONFSCI, SCISEARCH, JICST-EPLUS, PROMT, TOXLIT, TOXLINE, DRUGU,
     DRUGNL, DRUGLAUNCH, DRUGB, CANCERLIT, USPATFULL' ENTERED AT
     17:12:49 ON 07 DEC 1998)
L32          121 S ROSOK M?/AU
L33          326 S YELTON D?/AU
L34           33 S L32 AND L33
L35          101 S (L32 OR L33) AND L11
L36          112 S L34 OR L35
L37           11 S L35 AND TOXIC?
L38           39 S L34 OR L37
L39           15 DUP REM L38 (24 DUPLICATES REMOVED)

=> d 1-15 bib abs

L39  ANSWER 1 OF 15  CAPLUS  COPYRIGHT 1998 ACS        DUPLICATE 1
AN   1998:112463  CAPLUS
DN   128:204075
TI   A method for inhibiting immunoglobulin-induced
     toxicity resulting from the use of immunoglobulins
     in therapy and in vivo diagnosis
                         Searcher  :  Shears   308-4994
```

-Author (s)

IN **Rosok, Mae Joanne; Yelton, Dale E.**
PA Bristol-Myers Squibb Co., USA
SO PCT Int. Appl., 140 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9805787	A1	19980212	WO 97-US13562	19970801
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9739688	A1	19980225	AU 97-39688	19970801

PRAI US 96-23033 19960802
WO 97-US13562 19970801

AB The present invention provides a method for inhibiting **Ig** -induced **toxicity** resulting from immunotherapy in a subject comprising administering an **Ig** or **Ig** fusion protein mol. to the subject, the **Ig** mol. having a variable region and a const. region, the **Ig** mol. being modified prior to administration by inactivation of at least a portion of the const. region. The **Ig**. fusion protein is a **IgG**, **IgM**, or **IgA** which recognizes and binds Ley or Le. The **Ig**. fusion protein may also be labeled with radiolabel, enzyme, chromophore, chemiluminescer or fluorescer for tumor diagnosis, or conjugates to cytotoxic agent for cancer therapy. HBR96-2B, hBR96-2C, hBR96-2D, hBR96-2E, hBR96-2F, hBR96-2G, and hBR96-2H are provided for the diagnosis and therapy purposes.

L39 ANSWER 2 OF 15 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 2
AN 1998:545386 CAPLUS
DN 129:188362
TI Mutant BR96 antibodies reactive with human carcinomas
IN **Yelton, Dale**; Glaser, Scott; Huse, William; **Rosok, Mae Joanne**
PA Bristol-Myers Squibb Co., USA
SO U.S., 71 pp. Cont.-in-part of U. S. Ser. No. 285,936.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5792456	A	19980811	US 95-487860	19950607
US 5728821	A	19980317	US 94-285936	19940804
CA 2155397	AA	19960205	CA 95-2155397	19950803
AU 9528349	A1	19960215	AU 95-28349	19950803

EP 699756 A1 19960306 EP 95-305444 19950803
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
JP 08191692 A2 19960730 JP 95-230629 19950804
PRAI US 94-285936 19940804
US 95-487860 19950607
OS MARPAT 129:188362
AB The authors disclose the prepn. and improved reactivity of polypeptide muteins of the BR96 antibody directed to the Lewis Y determinant. Muteins were constructed using codon mutagenesis of heavy chain CDRs. Application of mutein immunoconjugates in cancer diagnosis and treatment is discussed.

L39 ANSWER 3 OF 15 USPATFULL
AN 1998:28198 USPATFULL
TI Mutant BR96 antibodies reactive with human carcinomas
IN **Yelton, Dale**, Seattle, WA, United States
Glaser, Scott, San Diego, CA, United States
Huse, William, Del Mar, CA, United States
Rosok, Mae Joanne, Seattle, WA, United States
PA Bristol-Myers Squibb Company, Princeton, NJ, United States (U.S. corporation)
PI US 5728821 980317
AI US 94-285936 940804 (8)
DT Utility
EXNAM Primary Examiner: Feisee, Lila; Assistant Examiner: Ungar, Susan
LREP Merchant, Gould, Smith, Edell, Welter & Schmidt
CLMN Number of Claims: 21
ECL Exemplary Claim: 1,4
DRWN 25 Drawing Figure(s); 23 Drawing Page(s)
LN.CNT 3197
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides mutant BR96 polypeptides (and nucleotide sequences encoding them) having a variable region comprising an amino acid sequence derived from the variable region of BR96.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L39 ANSWER 4 OF 15 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 3
AN 1998:134102 CAPLUS
DN 128:256176
TI Analysis of BR96 binding sites for antigen and anti-idiotype by codon-based scanning mutagenesis
AU **Rosok, Mae Joanne**; Eghtedarzadeh-Kondri, Mohammad; Young, Kelly; Bajorath, Jurgen; Glaser, Scott; **Yelton, Dale**
CS Bristol-Myers Squibb Pharmaceutical Research Institute, Seattle, WA, 98121, USA
SO J. Immunol. (1998), 160(5), 2353-2359

CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB We performed a scanning mutagenesis study of heavy chain complementarity-detg. region (CDR) residues to identify how mutations affected binding of the anti-carcinoma mAb BR96 to Ag, Lewis Y, and to an anti-Id Ab (anti-Id). By ELISA, we demonstrated that the anti-Id bound close to the Ag binding site of BR96, but the anti-Id and Ag sites were not identical. Immunoblot anal. and screening of light and heavy chain CDR libraries with multiple mutations in each CDR suggested that the heavy chain had greater involvement in anti-Id binding. We then analyzed contributions of individual residues in the heavy chain CDRs to binding of Ag and anti-Id. In as filamentous phage vector contg. BR96 V region sequences, mutations were introduced by codon-based mutagenesis at single positions within the three heavy chain CDRs. The resulting libraries of Fab fragments had all amino acids represented at a CDR position. We evaluated the expressed Fabs for binding to Ag and anti-Id by plaque lift assay. We identified the positions with mutations that had the greatest neg. effect on binding to the anti-Id and to Ag and analyzed them on the basis of the BR96 x-ray structure. The residues most important for binding to the anti-Id were located in heavy chain CDR1 and CDR2 and were peripheral to the residues within the Lewis Y binding pocket.

L39 ANSWER 5 OF 15 USPATFULL
AN 97:78179 USPATFULL
TI Monoclonal antibody compositions cross-reactive and cross-protective against P. aeruginosa serotypes
IN Siadak, Anthony W., Seattle, WA, United States
Rosok, Mae J., Seattle, WA, United States
PA Bristol-Myers Squibb Company, New York, NY, United States (U.S. corporation)
PI US 5662905 970902
AI US 94-366204 941229 (8)
RLI Continuation of Ser. No. US 93-66604, filed on 24 May 1993, now patented, Pat. No. US 5378812 which is a continuation of Ser. No. US 86-931179, filed on 24 Nov 1986, now abandoned which is a continuation-in-part of Ser. No. US 85-807394, filed on 10 Dec 1985, now abandoned
DT Utility
EXNAM Primary Examiner: Loring, Susan A.
LREP Townsend And Townsend And Crew LLP
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1412
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Cell lines have been produced that secrete human monoclonal antibodies capable of binding to the lipopolysaccharide molecules of selected Pseudomonas aeruginosa IATS serotypes. Pharmaceutical compositions containing these antibodies, which can be in combination with other monoclonal antibodies, blood plasma fractions and antimicrobial agents, and the prophylactic and therapeutic use of such compositions in the management of infections are included. Prior to filing of this patent application the continuous transformed human cell lines 1C1, 6D6 and 8H7 described herein were deposited in the American Type Culture Collection and given the designations CRL 8941, 9171, and 9258, respectively.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L39 ANSWER 6 OF 15 USPATFULL
AN 97:40481 USPATFULL
TI Method for inhibiting the viability of Pseudomonas aeruginosa with cross-reactive and cross-protective monoclonal antibodies
IN Siadak, Anthony W., Seattle, WA, United States
Rosok, Mae J., Seattle, WA, United States
PA Bristol-Myers Squibb Company, New York, NY, United States (U.S. corporation)
PI US 5628996 970513
AI US 95-463910 950605 (8)
RLI Division of Ser. No. US 94-366204, filed on 29 Dec 1994 which is a continuation of Ser. No. US 93-66604, filed on 24 May 1993, now patented, Pat. No. US 5378812 which is a continuation of Ser. No. US 86-931179, filed on 24 Nov 1986, now abandoned which is a continuation-in-part of Ser. No. US 85-807394, filed on 10 Dec 1985, now abandoned
DT Utility
EXNAM Primary Examiner: Housel, James C.; Assistant Examiner: Loring, Susan A.
LREP Townsend and Townsend and Crew LLP
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1405
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Cell lines have been produced that secrete human monclonal antibodies capable of binding to the lipopolysaccharide molecules of selected Pseudomonas aeruginosa IATS serotypes. Pharmaceutical compositions containing these antibodies, which can be in combination with other monoclonal antibodies, blood plasma fractions and antimicrobial agents, and the prophylactic and therapeutic use of such compositions in the management of infections are included.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L39 ANSWER 7 OF 15 USPATFULL
AN 97:38410 USPATFULL
TI Monoclonal antibodies cross-reactive and cross-protective against human monoclonal antibodies against pseudomonas aeruginosa serotypes
IN Siadak, Anthony W., Seattle, WA, United States
Rosok, Mae J., Seattle, WA, United States
PA Bristol-Myers Squibb Company, New York, NY, United States (U.S. corporation)
PI US 5627067 970506
AI US 95-462370 950605 (8)
RLI Division of Ser. No. US 94-366204, filed on 29 Dec 1994 which is a continuation of Ser. No. US 93-66604, filed on 24 May 1993, now patented, Pat. No. US 5378812 which is a continuation of Ser. No. US 86-931179, filed on 24 Nov 1986, now abandoned which is a continuation-in-part of Ser. No. US 85-807394, filed on 10 Dec 1985, now abandoned
DT Utility
EXNAM Primary Examiner: Loring, Susan A.
LREP Townsend and Townsend and Crew
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1391
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Cell lines have been produced that secrete human monclonal antibodies capable of binding to the lipopolysaccharide molecules of selected Pseudomonas aeruginosa IATS serotypes. Pharmaceutical compositions containing these antibodies, which can be in combination with other monoclonal antibodies, blood plasma fractions and antimicrobial agents, and the prophylactic and therapeutic use of such compositions in the management of infections are included.

Prior to filing of this patent application the continuous transformed human cell lines 1C1, 6D6, and 8H7 described herein were deposited in the American Type Culture Collection and given the designations CRL 8941, 9171, and 9258, respectively.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L39 ANSWER 8 OF 15 BIOTECHDS COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 96-05132 BIOTECHDS
TI New mutant BR96 polypeptides;
monoclonal antibody and chimeric antibody engineering; protein engineering for increased affinity for Lewis-Y tumor-associated antigen; use in cancer diagnosis and therapy

AU **Yelton D**; Glaser S; Huse W; **Rosok M J**
PA Bristol-Squibb
LO New York, NY, USA.
PI AU 9528349 15 Feb 1996
AI AU 95-28349 3 Aug 1995
PRAI US 95-487860 7 Jun 1995; US 94-285936 4 Aug 1994
DT Patent
LA English
OS WPI: 96-129723 [14]
AN 96-05132 BIOTECHDS
AB A new mutant BR96 protein contains a protein sequence including specified sequences in a complementarity determining region (CDR), heavy chain variable region and more specifically CDR1, CDR2 and CDR3. The protein may be a monoclonal antibody, chimeric antibody, Fab, F(ab')2 or Fv fragment. DNA encoding the protein (e.g. cDNA) may be inserted in a plasmid vector for expression in a host cell, e.g. Escherichia coli or a eukaryote. The mutant BR96 antibody may be produced by mutagenesis of DNA encoding BR96 and purification from a recombinant host. The mutant BR96 antibody has an increased affinity for the Lewis-Y antigen, which is expressed by carcinomas and some different epithelial cells, as compared to native BR96. The antibody may be used in cancer diagnosis, or in production of conjugate immunotoxins with cytostatic activity against cancer or proliferative disease. (108pp)

L39 ANSWER 9 OF 15 CAPLUS COPYRIGHT 1998 ACS
AN 1996:222491 CAPLUS
DN 124:250918
TI Novel mutant BR96 monoclonal antibodies, their production using plasmids, and their application as immunoconjugates with cytotoxic agents in human carcinoma treatment
IN **Yelton, Dale**; Glaser, Scott; Huse, William; **Rosok, Mae Joanne**
PA Bristol-Myers Squibb Company, USA
SO Eur. Pat. Appl., 91 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 699756	A1	19960306	EP 95-305444	19950803
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	US 5728821	A	19980317	US 94-285936	19940804
	US 5792456	A	19980811	US 95-487860	19950607
PRAI	US 94-285936	19940804			
	US 95-487860	19950607			

AB The present invention provides mutant BR96 polypeptides (and cDNAs

encoding them) having a variable region comprising an amino acid sequence substantially homologous to the variable region of monoclonal antibody BR96. Immunoconjugates, BR96 mutants conjugated with cytotoxic agents have applications in treatments of human carcinomas.

L39 ANSWER 10 OF 15 TOXLIT
AN 1996:76175 TOXLIT
DN CA-124-250918S
TI Novel mutant BR96 monoclonal antibodies, their production using plasmids, and their application as immunoconjugates with cytotoxic agents in human carcinoma treatment.
AU **Yelton D**; Glaser S; Huse W; **Rosok MJ**
SO (1996). Eur. Pat. Appl. PATENT NO. 699756 03/06/96 (Bristol-Myers Squibb Company).
CY United States
DT Patent
FS CA
LA English
OS CA 124:250918
EM 199605
AB The present invention provides mutant BR96 polypeptides (and cDNAs encoding them) having a variable region comprising an amino acid sequence substantially homologous to the variable region of monoclonal antibody BR96. Immunoconjugates, BR96 mutants conjugated with cytotoxic agents have applications in treatments of human carcinomas.

L39 ANSWER 11 OF 15 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 5
AN 1996:572221 CAPLUS
DN 125:218995
TI A combinatorial library strategy for the rapid humanization of anticarcinoma BR96 Fab
AU **Rosok, Mae Joanne; Yelton, Dale E.**; Harris, Linda J.; Bajorath, Jurgen; Hellstrom, Karl-Erik; Hellstrom, Ingegerd; Cruz, Gina A.; Kristensson, Karin; Lin, Huey; et al.
CS Bristol-Myers Squibb Pharmaceutical Res. Inst., Seattle, WA, 98121, USA
SO J. Biol. Chem. (1996), 271(37), 22611-22618
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB The authors have used a combinatorial mutagenesis strategy to humanize BR96, a monoclonal antibody that binds to the Lewis Y class of tumor antigens. This approach allows simultaneous assessment of hundreds of humanized variable regions to identify the mols. that best preserve affinity, thus overcoming the major drawback of current humanization procedures, the requirement to construct and analyze each humanized antibody sep. Murine residues of BR96 were

mutated to human if they were solvent-exposed residues that did not participate in the formation of the antigen binding site and were not at the interface of the light and heavy chain. At positions that might be involved in binding to antigen, the choice between the murine and human residue was more difficult. Murine and human alternatives were incorporated into a combinatorial library at positions representing buried residues that might affect the structural integrity of the antigen binding site. By encoding this library of humanized BR96 Fabs in an M13 phage vector, the authors rapidly identified several candidates with nearly identical antigen binding, within 2-fold, of the chimeric Fab. Addnl. mutagenesis directed at sites suggested in the literature as potentially important for antigen binding in a similar anti-Lewis Y antibody yielded no further improvements.

L39 ANSWER 12 OF 15 USPATFULL
AN 95:1714 USPATFULL
TI Monoclonal antibodies cross-reactive and cross-protective against P. aeruginosa serotypes
IN Siadak, Anthony W., Seattle, WA, United States
Rosok, Mae J., Seattle, WA, United States
PA Bristol-Myers Squibb Company, New York, NY, United States (U.S. corporation)
PI US 5378812 950103
AI US 93-66604 930524 (8)
RLI Continuation of Ser. No. US 86-931179, filed on 24 Nov 1986, now abandoned which is a continuation-in-part of Ser. No. US 85-807391, filed on 10 Dec 1985, now abandoned
DT Utility
EXNAM Primary Examiner: Lacey, David L.; Assistant Examiner: Loring, Susan A.
LREP Townsend and Townsend Khourie and Crew
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1363
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Cell lines have been produced that secrete human monclonal antibodies capable of binding to the lipopolysaccharide molecules of selected Pseudomonas aeruginosa IATS serotypes. Pharmaceutical compositions containing these antibodies, which can be in combination with other monoclonal antibodies, blood plasma fractions and antimicrobial agents, and the prophylactic and therapeutic use of such compositions in the management of infections are included.

Prior to filing of this patent application the continuous transformed human cell lines 1C1, 6D6, and 8H7 described herein were deposited in the American Type Culture Collection and given

the designations CRL 8941, 9171, and. 9258, respectively.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L39 ANSWER 13 OF 15 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 6
AN 1995:740198 CAPLUS
DN 123:141273
TI Affinity maturation of the BR96 anti-carcinoma antibody by codon-based mutagenesis
AU **Yelton, Dale E.**; **Rosok, Mae Joanne**; Cruz, Gina; Cosand, Wesley L.; Bajorath, Juergen; Hellstroem, Ingegerd; Hellstroem, Karl Erik; Huse, William D.; Glaser, Scott M.
CS Bristol-Myers Squibb Pharmaceutical Res. Inst., Seattle, WA, 98121, USA
SO J. Immunol. (1995), 155(4), 1994-2004
CODEN: JOIMA3; ISSN: 0022-1767
DT Journal
LA English
AB We have increased up to 65-fold the avidity of BR96, a mAb recognizing Lewis Y (Ley)-related Ags expressed on the surface of many human carcinomas. Libraries of mutations in the complementarity-detg. regions (CDRs) of BR96 were constructed in an M13 phage Fab expression vector by codon-based mutagenesis, a method that efficiently introduces large nos. and potentially all combinations of amino acid substitutions. Two mutants that improved the affinity of BR96 to tumor Ag were identified by screening the libraries on carcinoma cell lines. One mutant, M1, at position 97 (Asp to Ala) in CDR3 of the heavy chain, resulted in an 8- to 10-fold improvement in Ag binding, as assessed by ELISA. A second mutant, M2, at position 53 (Gly to Asp) in CDR2 of VH increased binding three- to fivefold. When these mutations were combined, the resulting Fab M3 was improved approx. 30-fold. An addnl. library was constructed in CDR1 of M1. M4, a mutation with three amino acid substitutions in CDR1, was isolated by screening the library with an enzyme conjugate of synthetic Ley tetrasaccharide (sLey). This mutant improved BR96 Fab affinity to sLey an estd. 15- to 20-fold by ELISA, and 14-fold as measured by surface plasmon resonance. The M4 IgG had 65-fold improved avidity to sLey relative to the BR96 IgG. The mutants will be useful for comparison of the efficacy of Abs with different affinities for delivery of cytotoxic agents to tumor cells.

L39 ANSWER 14 OF 15 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 90-48785 DRUGU T S
TI Phase I Trial of Chimeric Monoclonal Antibody L6 (ChL6).
AU Goodman G E; Murray J L; Hellstrom K E; Nicaise C; **Yelton D** ; Palazollo P
LO Seattle, Washington, Houston, Texas, Wallingford, Connecticut, United States

Searcher : Shears 308-4994

SO Proc.Am.Assoc.Cancer Res. (31, 81 Meet.; 174, 1990) ISSN: 0197-016X
AV Swedish Hospital Tumor Institute, Seattle, WA, U.S.A. (8 authors).
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 90-48785 DRUGU T S
AB In a phase I trial of 17 patients with breast, colon, ovary and lung cancers, a single i.v. infusion of a chimeric monoclonal antibody L6 (ChL6), was associated with severe headaches and fever at higher doses. ChL6 remained in the serum and was present on tumor cells for several days. (congress abstract).
ABEX Methods ChL6 was given to 17 patients as a single 4-18 hr i.v. infusion at dose levels of 35, 70, 140, 350 and 700 mg/sq.m. Results Patients receiving doses over 140 mg/sq.m developed severe headaches and fever which lasted 12-48 hr. No laboratory evidence of **toxicity** was observed. Serum complements fell within 24 hr and remained low for 2 wk. ChL6 serum half-life was 4-5 days. Biopsies at 3 days showed localization at doses above 70 mg/sq.m and saturation at 700 mg/sq.m. On day 7, ChL6 was still present on tumor cells. Human anti-mouse antibody was detected in 1 patient. (E61/MB)

L39 ANSWER 15 OF 15 USPATFULL
AN 89:43140 USPATFULL
TI Monoclonal antibodies to pseudomonas aeruginosa flagella
IN **Rosok, Mae J.**, Seattle, WA, United States
Lostrom, Mark E., Redmond, WA, United States
PA Genetic Systems Corporation, Seattle, WA, United States (U.S. corporation)
PI US 4834976 890530
AI US 86-946554 861224 (6)
RLI Continuation-in-part of Ser. No. US 86-881984, filed on 3 Jul 1986
DT Utility
EXNAM Primary Examiner: Warden, Robert J.; Assistant Examiner: Wagner, Richard
LREP Townsend and Townsend
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1574
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Cell lines have been produced that secrete monoclonal antibodies capable of binding to the flagellar proteins of selected Pseudomonas aeruginosa strains. Some of these antibodies have been found to be protective against lethal challenges of P. aeruginosa. Pharmaceutical compositions containing these antibodies, which can be in combination with other monoclonal antibodies, blood plasma

fractions and antimicrobial agents, and the prophylactic and therapeutic use of such compositions in the management of infections, are included.

Prior to filing this application, the continuous transformed cell lines PaF4 IVE8, FA6 IIG5, 20H11, and 21B8, described herein, were deposited in the America Type Culture Collection and given the designations HB9129, HB9130, CRL 9300, and CRL 9301, respectively.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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